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Chapter 4: Green Engineering
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Chapter 5: Process Intensification in the Chemical Industry: A Review
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Green Engineering

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4.1 Introduction: Green Engineering Misconceptions and Realizations

During your career you have likely come across a colleague or co-worker who held the opinion that any greener alternative to a current process, chemical, or product is 1) more expensive, 2) doesn't work as well, or 3) is only motivated by external regulation [1]. This misconception is a primary argument of those opposing green innovation, but highlights that any greener alternative will not be adopted unless it is economically justified and does not sacrifice function [2]. Examples of such innovation are broad reaching across many aspects of the chemical industry as evidenced by the Presidential Green Chemistry Challenge Award winners [3]. It must also be realized that 1) the economics must be evaluated over the entire life cycle and 2) it is always better to incorporate greener alternatives in the design stage, rather than having to retrofit existing processes. Often different design stages of chemical processes are conducted independently thus hindering their systemic evaluation and possibly squandering opportunities for improvement. For example, the choice of raw materials, solvents, or reaction pathway is done based on operating costs that maximize the economic differential between product and consumables, including energy. If this is done before a rigorous evaluation of the capital and operating costs associated with separations, waste generation and treatment, fugitive emissions, safety measures, and risk assessment, then it is quite possible that a greener and more economical alternative is overlooked.

In order to avoid this opportunity loss and not handicap a process design with initial design choices, it is imperative to incorporate both guiding green engineering design principles as well as quantifiable green chemistry metrics with conventional design tools in the initial design stages [4]. While the economic advantage of a greener alternative may not be evident in preliminary design, advantages may emerge later during risk assessment analysis. Risk assessment is a systematic process of evaluating the probability of any event with adverse implications and the potential loss associated with each event, including economic loss. A comprehensive risk assessment by itself requires significant effort, time and expense, thus it is prohibitive to conduct during the early stages of a process design. Understanding the potential implications of design choices on risk assessment is reasonable and if done correctly, can streamline the overall design process by avoiding scenarios that require significant risk assessment. This is the concept of inherently safer design; Green Engineering Principle #1 [5].

Green engineering is defined by the U.S. Environmental Protection Agency as "the design, commercialization, and use of processes and products in a way that reduces pollution, promotes sustainability, and minimizes risk to human health and the environment without sacrificing economic viability and efficiency [6]." This is a working definition that has evolved to focus on a risk aversion viewpoint that weighs both human health

Green Techniques for Organic Synthesis and Medicinal Chemistry, Second Edition. Edited by Wei Zhang and Berkeley W. Cue.

and the environment [7]. The definition also places emphasis on sustainability from an economic standpoint, which reinforces the concept that any green engineering alternative must also be economical.

4.2 12 Principles of Green Engineering

Complementing the seminal publication by Anastas and Warner that defined the 12 Principles of Green Chemistry [8]. Anastas and Zimmerman later published the 12 Principles of Green Engineering, which are presented in abbreviated form [5]. Each of these benchmark principles focuses on different life-cycle stages of the engineering design or improvement process spanning from raw material and energy sources to end of life; systems design to process intensification. In all, the 12 Principles can be categorized into reducing hazard, increasing efficiency, minimizing excess, and increasing sustainability.

Many of the Principles are more straight forward to understand, others are less obvious, such as (3) design for separations, (5) output pulled, (6) reduce complexity, (9) minimize material diversity, and (8) avoid excess capacity. Typically, 70% of the materials and energy in a process are dedicated to separations, and generally the separation is designed based on the upstream process. A *design for separations* approach seeks to enhance efficiency by crafting the upstream such that the downstream separation requires less energy and materials. The end result may require increased upstream cost (e.g., in a reactor system), but the reduced separations cost will result in a decreased net cost. The concept of *"output pulled"* is derived from Le Chatelier's Principle, where a process should be developed in the direction which exploits equilibrium. In other words, a process will proceed more efficiently along a minimization of the Gibbs free energy, or it is easier to paddle down a river with the current versus against the current. *Reducing complexity, minimizing material diversity, and reducing capacity* can each be viewed as steps toward risk reduction. In such cases, increased complexity leads to higher probability that an unforeseen adverse event can occur; increased material diversity leads to potential chemical incompatibilities or reduced ability for material reuse; and excess capacity leads to greater potential for accidental spills or releases.

The 12 Principles of Green Engineering

1) Strive for inherently nonhazardous materials and energy inputs.
2) Prevent waste rather than treat.
3) Design separations and purifications to minimize energy and materials consumption.
4) Maximize mass, energy, space, and time efficiency.
5) "Output Pulled" rather than "Input Pushed".
6) Reduce complexity.
7) Design for durability, not immortality.
8) Avoid unnecessary capacity or capability.
9) Minimize material diversity.
10) Integration of energy and material flows.
11) Design for commercial afterlife.
12) Renewable rather than depleting.

The 12 Principles of Green Engineering serve as guidelines by which to develop a mindset conducive toward inherently greener products and processes. While these Principles inherently address several conventional design goals – maximizing profits, increasing energy efficiency, and use of safeguards to manage hazards – adherence to these Principles can provide additional guidance toward greener, safer, and more sustainable products or processes.

4.3 Green Chemistry Metrics Applied to Engineering

A practicing chemical engineer may say: “In my plant we strive to maximize efficiency, recover and recycle solvents and reactants, recover waste heat, use catalysts, and minimize toxic releases to the environment. Are we not Green Engineers?” Reply: YES. These are aspects of Green Engineering that are driven by economics. Now ask yourself: What happens at the product’s end of life? Where are the raw materials sourced from? What happens when an accidental exposure or release does occur? Can we do better? YES. How can we do better? In order to answer this question, we need metrics to be able to perform quantitative evaluation of existing processes or products and new alternatives.

A metric is a quantifiable standard of measure that can be used for comparison. Green chemistry metrics can be used to determine if one product or process is “greener” than another (Comparative) or identify aspects of a product or process that can be improved (Improvement). Many green chemistry metrics exist, as discussed in previous chapters; the challenge is to choose the most appropriate.

The types of metrics that can be implemented span from very simplistic to extremely complex. Simple metrics are useful for rapid, transparent, and direct comparisons of similar scenarios, which can be used to easily display advantages of one reaction, process, or product over another. These green chemistry metrics include atom economy, E-factor, effective mass yield, reaction mass efficiency, environmental index, and so on. Conventional metrics that are on the same level of complexity include reaction yield, which is a product of reaction conversion and selectivity or cost index. Cost index (CI) is a baseline economic analysis that compares the cost of products to reactants: $\mathrm{CI} = \sum -\nu * \textit{Cost per pound or mole}$; where ν is the mass or mole stoichiometric factor. Similar to the Green Chemistry metrics, the cost index can be very useful in an initial cursory comparison of two very similar scenarios but neglect significant details as a trade-off for ease of implementation. As an example, Environmental Index (EI) can be used is a similar manor to CI where $\mathrm{EI} = \sum |\nu| * \textit{Toxicity Factor}$; where *Toxicity Factor* can be defined as the inverse of a conventional toxicity measures such as a threshold limit value (TLV), permissible exposure limit (PEL), or recommended exposure limit (REL). For EI comparisons, a smaller number is preferred and thus the reciprocal of the toxicity measure is used. Furthermore, for more toxic compounds, there can be little difference in the numerical value but the reciprocal will have greater difference. The inverse is true for less toxic compounds. Also, the absolute value of the stoichiometric factor is used because unlike the CI, toxicity can result from exposure to reactants or products and they are always present.

Traditional Tools	Green Chemistry Tools
• Level 1 – Yield and Selectivity – Row Materials Cost – Energy Requirements – Product Price – Waste Treatment	• Level 1 – E-Factor – Atom Economy – Effective Mass Yield – Reaction Mass Efficiency – Environmental Index
• Level 2 – Process Optimization – Process Integration	• Level 2 – Routes to Exposure – Hazard Assessment
• Level 3 – Process Design – Risk Analysis	• Level 3 – Risk Analysis – Life Cycle Assessment – Sustainability Analysis

A second level of Green Chemistry metrics contains an increase in complexity as well as depth of evaluation. These include a higher level of specific hazard assessment and potential routes of exposure. Specific hazard analysis can include methods such as What If Analysis (WIA), Fault Tree Analysis (FTA), or Failure Mode and Effect Analysis (FMEA). FTA is a deductive, top-down method while FMEA is an inductive, bottom-up method. Regardless of the method, the result is identification of individual potential routes of failure with a certain probability of resulting in an adverse effect. The magnitude of the adverse effect for chemical hazards is a function of the toxicity, route to exposure, and exposure concentration. Exposure concentration is determined by a balance of time dependent release rate, transport, and degradation rate. Compilations of these metrics are a component of a full risk assessment, which is categorized as a Level 3 metric.

4.3.1 Maleic Anhydride Production Example

Maleic anhydride (MA) is classified as a commodity chemical with global production in excess of 1.5 million tons per year [1, 9]. It is primarily used in the manufacture of polyester resins for commercial applications in construction, marine, automotive, textiles, and consumer products applications. It is also widely used as a chemical precursor in the agricultural and chemicals industries, as well as in the food, consumer goods, and personal care products industries.

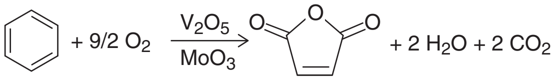
MA was first produced industrially in the 1930s by vapor-phase catalytic oxidation of benzene over a vanadium oxide and molybdenum oxide catalyst. Due to the ease of oxidation and high selectivity for MA, the benzene process dominated global production until the early 1980s. Rapidly increasing costs and growing environmental concerns associated with benzene use motivated a transition to an alternate feedstock. Furthermore, benzene conversion is inherently inefficient due to the conversion of a C_6 feedstock to a C_4 product (lower atom economy). This resulted in the exploration of C_4 feedstocks, and a process to produce MA from low-cost n-butane. Monsanto built the first butane to MA plant in 1974 and by the mid-1980s, 100% of U.S. production was from butane. Despite having lower selectivity, the butane process was preferred due to the lower feedstock cost, decreased environmental impact, and increased atom economy. The increased atom economy results in a competitive mass yield for butane with the lower selectivity. Advancements in catalysts for the butane reaction increased activity to enable conversion of benzene-based plants without capacity loss. Further advancements led to more energy efficient, solvent-based isolation and purification methods [9].

4.3.2 Level 1 Green Chemistry Metrics

Figure 4.1 shows the two chemical reactions for converting benzene and n-butane to MA. Both reactions are catalytic oxidation reactions with a single reaction step that can be evaluated using Level 1 green chemistry metrics. The benzene reaction has an E-factor of 1.26, atom economy of 0.44 and EI of 5.6 based on the TLV values. In contrast, the n-butane reaction has an E-factor of 0.73, atom economy of 0.58, and EI of 4.0. Based on these metrics, the n-butane process is preferred, but stoichiometric factor, conversion, selectivity, and yield are not accounted for.

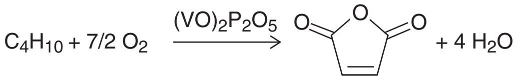
Quinone is a by-product of the benzene oxidation reaction and to avoid quinone production, the reaction is run with excess oxygen at a 13.5:1 ratio rather than the stoichiometric 4.5:1 ratio. This excess results in lower MA yield due to CO_2 formation but reduces quinone and results in a stoichiometric factor of 2.3 and a yield of 62%. The n-butane route has a decreased MA selectivity of 55% and n-butane conversion of 85%, which results in a yield of 47%, but the use of excess reagents is not needed. The reaction mass efficiency (RME) metric can be used to compare these two routes in order to take into account, not only yield, but also excesses and other materials consumption. In this example the n-butane route (RME 0.270, assuming stoichiometric feeds and material recycle) has a more favorable RME than the benzene route (RME 0.122) despite the lower reaction yield. While a more detailed metric, the RME is still limited in scope and does not account for many other factors that will influence the comparative analysis, especially scale-up, and purification.

An alternate approach to the Level 1 metrics is to apply the same metrics to an industrial scale process, rather than chemical reactions and benchtop reaction yields, however, industrial scale data or simulations benzene to maleic anhydride



	Benzene	Oxygen	Maleic Anhydride	Water	Carbon Dioxide
MW (g/mol)	78.1	32.0	98.1	18.0	44.0
Stoichiometric Mass Ratio	0.80	1.47	1.0	0.37	0.90
TLV (ppm)	0.5	–	0.25	–	5000
PEL (ppm)	1–5	–	0.25	–	–
REL (ppm)	0.1	–	0.25	–	–

n-butane to maleic anhydride



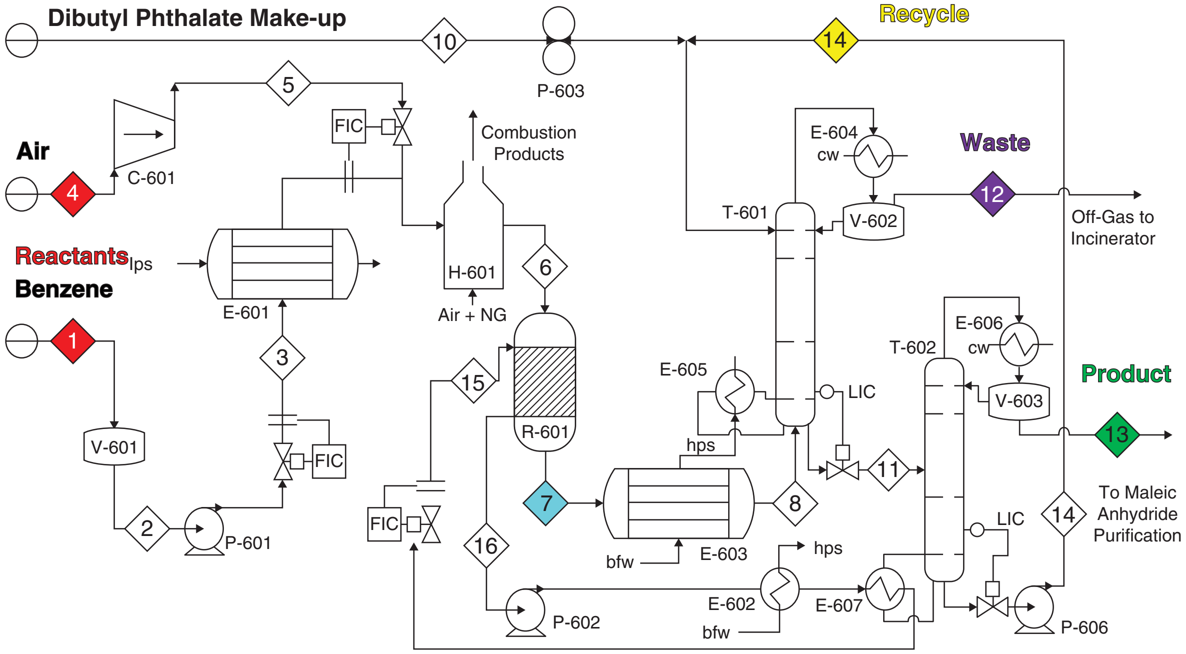
	n-butane	Oxygen	Maleic Anhydride	Water
MW (g/mol)	58.1	32.0	98.1	18.0
Stoichiometric Mass Ratio	0.59	1.14	1.0	0.73
TLV (ppm)	1000	–	0.25	–
PEL (ppm)	800	–	0.25	–
REL (ppm)	800	–	0.25	–

Figure 4.1 Comparison of the benzene and n-butane methods of MA synthesis with information needed for green chemistry metrics. Threshold Limit value (TLV), permissible exposure limit (PEL), and recommended exposure limit (REL) were obtained from safety data sheets.

may be difficult to obtain. Figure 4.2 shows an example process flow diagram (PFD) and process stream composition flows for an industrial scale benzene conversion to MA obtained from Turton *et al.* [1]. Benzene is mixed with excess air before being heated to 460°C and fed into a vapor-phase reactor where the exothermic catalytic oxidation reaction occurs. Excess air is used to suppress by-product formation and avoid the lower flammability limit. The reaction product is then sent to an absorber and separation tower that uses dibutyl phthalate to isolate the MA.

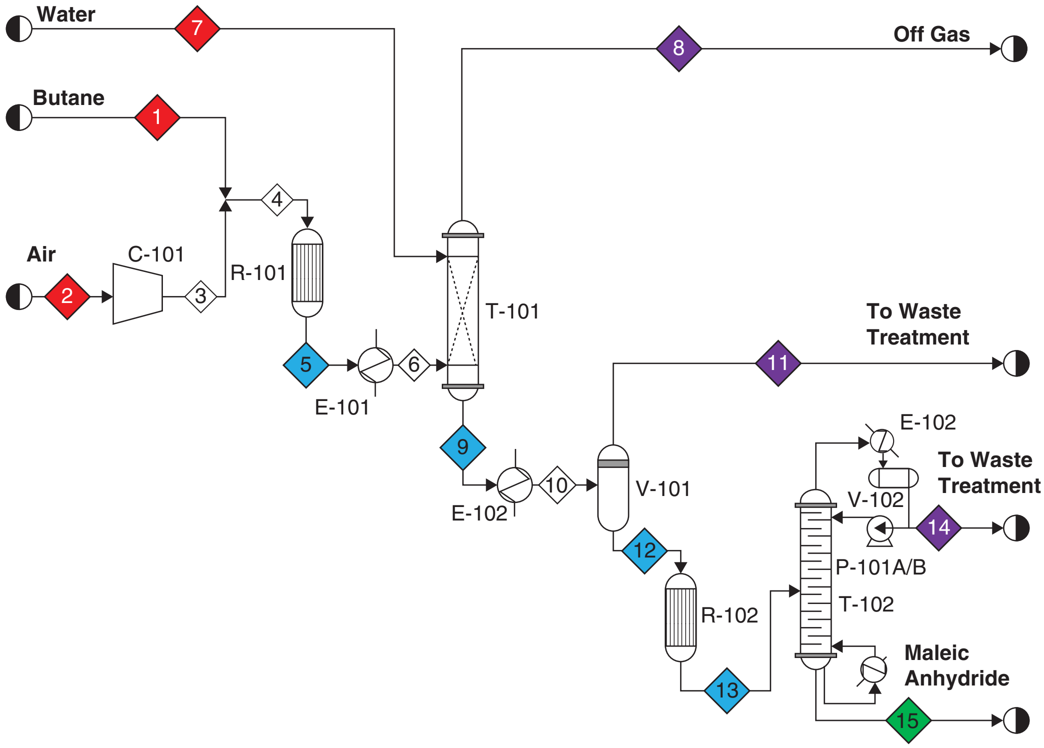
A mass-based E-factor of 31.3 can be determined by taking the ratio of waste (stream 12) to product (stream 13). Stream 12 includes the inert N_2 from the air stream which could be argued is not a waste material. Without the N_2 inert, the E-factor becomes 7.5. Further analysis of the PFD gives a MA yield of 62% around the primary reactor, an overall yield of 59%, and a stoichiometric factor of 2.34. Assuming a materials recovery parameter of 1, gives an RME of 0.114.

Figure 4.3 is a PFD for the n-butane process. An E-factor of 20.5 is calculated from the ratio of waste streams 8, 11, and 14 to product stream 15. Neglecting the N_2 inert gives and E-factor of 8.18. The MA yield around the primary reactor is 78.7%, the overall yield is 74.6%, and the stoichiometric factor is 1.97. Assuming a materials recovery parameter of 1, yields a RME of 0.218.



Stream No.	1	4	6	7	8	9	10	11	12	13	14
Temperature (°C)	30	30	460	608	260	329	320	194	84	189	329
Pressure (kPa)	101	101	235	220	215	80	100	82	75	70	80
Total (kmol/h)	42.3	2790	2832.3	2825.2	2825.3	500.1	0.1	526.2	2797.9	26.2	500
Total (kg/h)	**3304**	**80490**	83794	83794	83794	139191.6	30.6	141866	81225	**2597**	139269
Flowrates (kmol/h)											
Maleic Anhydride	–	–	0	**26.3**	26.3	–	–	24.8	0.5	**24.8**	–
Dibutyl Phthalate	–	–	0	–	–	500.5	0.1	500.4	0.1	–	500.4
Nitrogen	–	2205	2205	2205	2205	–	–	–	2205	–	–
Water	–	–	0	91.5	91.5	–	–	–	90.5	–	–
Oxygen	–	**585**	585	370.2	370.2	–	–	–	370.2	–	–
Benzene	**42.3**	–	42.3	**2.6**	2.6	–	–	–	2.6	–	–
Quinone	–	–	–	0.7	0.7	–	–	0.4	0.4	0.4	–
Carbon Dioxide	–	–	0	129	129	–	–	–	129	–	–
Maleic Acid	–	–	0	–	–	–	–	1	–	1	–

Figure 4.2 Process flow diagram for the benzene to maleic anhydride process with composition information for the chemical streams throughout the process. Data for this figure and the PFD were obtained from Turton *et al.* [1]. *Source*: Adapted from Turton, 2008.



Stream No.	1	2	5	7	8	9	11	12	13	14	15
Temp. (°C)	20	20	410	45	59.9	60	120	120	160	97.1	162
Press. (kPa)	275	101	275	170	170	170	101	101	101	101	101
Vapor Fraction	0	1	1	0	1	0	1	1	0.7	0	0
Flowrate (kg/h)	2000	41174	43174	11216	37621	16769	13640	3128.8	3128.8	602.5	2526.3
Flowrates (kmol/h)											
Nitrogen	–	1115	1115	–	1115	–	–	–	–	–	–
Carbon Monoxide	–	–	0.78	–	0.78	–	–	–	–	–	–
Oxygen	–	297	196	–	196	–	–	–	–	–	–
Carbon Dioxide	–	–	2.3	–	2.3	–	–	–	–	–	–
Butane	34.4	–	6.1	–	–	6.1	6.1	.002	.002	.002	.–
Water	–	25.2	138	623	–	138	734	0.7	27.6	27.3	0.25
Formic Acid	–	–	0.39	–	–	0.39	0.38	.004	.004	.004	.002
Acrylic Acid	–	–	0.39	–	–	0.39	0.37	0.02	0.02	.008	0.01
Maleic Anhydride	–	–	27.1	–	–	27.1	–	–	26.8	1.1	25.7
Maleic Acid	–	–	–	–	–	–	0.29	26.9	–	–	–

Figure 4.3 Process flow diagram for the n-butane to maleic anhydride process with composition information for the chemical streams throughout the process. This figure is adapted from Turton and Shaeiwitz [2]. *Source*: Adapted from Turton, 2008 and Shaeiwitz, 2017.

Table 4.1 Summary of Level 1 Green Chemistry metrics applied to the maleic anhydride reactions and process flow diagrams for the benzene and n-butane processes.

Metric	Benzene Process	Butane Process
Chemical Reaction		
E-factor (MW)	1.27	**0.734**
Atom Economy	0.454	**0.577**
Environmental Index	5.60	**4.00**
Yield	**0.62**	0.468
Reaction Mass Efficiency	0.122	**0.270**
Chemical Process (PFD)		
E-factor (mass)	**7.5**	8.18
Yield	0.62	**0.787**
Reaction Mass Efficiency	0.114	**0.281**
Environmental Index	5.46	4.0

Table 4.1 provides a summary of the Level 1 Green Chemistry metrics. When applied to the industrial scale PFD, the n-butane process has the advantage in yield, RME, and environmental index. The benzene process has a lower E-factor when N_2 is neglected, which results from the extensive water use in the purification stage. Potential for process improvement may include recycle of the water, as is done with the dibutyl phthalate in the benzene process.

Level 1 metrics can be very useful in a comparative analysis or identification of opportunities for improvement when complemented with conventional metrics that include energy consumption, and cost analysis. These metrics are also congruent with the Green Engineering Principles; specifically, Principles 1 through 4. Additional Level 1 metrics can also be envisioned which account for factors such as environmental persistence, bioaccumulation, bioconcetration, and so on.

4.3.3 Level 2 Green Chemistry Metrics

While conventional Level 2 design metrics may be seen as equivalent to process optimization or intensification, Green Chemistry metrics focus more on quantifying hazards and exposure in the occupational setting as well as the environment. The added complexity and diversity of contributing factors associated with the upper-level metrics often results in less quantitative tools and a greater proportion of qualitative assessment, which eventually boils down to cost and risk. Specific methods that can be used to conduct Level 2 analysis are well developed and broadly applicable techniques that are amenable to this level of evaluation.

RISK: In the context of a chemical plant, risk assessment can be evaluated as a cross product between hazard and exposure where the probability of an adverse event occurring and the severity of implications is a function of both the type of hazard and route or likelihood of exposure.

HAZARD: Hazards can exist in many forms as physical (e.g., pressure, temperature, velocity, electrical) or chemical. Within the chemical realm, hazards include toxicity, reactivity (corrosive, oxidizing, or explosive), flammability, or radioactivity. The hazard assessment essentially distills down to the different species present and the inherent hazards, which are a function of the physical properties (volatility, boiling point, water solubility, Henry's constant or octanol-water partition coefficient) or chemical properties (toxicity, reactivity, etc.), which can be measured or predicted. The above-mentioned hazards are what we can consider as conventional measures; from the green engineering standpoint, we must also consider environmental measures such as aquatic toxicity, bioaccumulation, bioconcentration, or potential for ecosystem disruption (global warming, ozone deletion, smog formation, acid rain, or eutrophication).

Now, to put the complexity of the issue into perspective, the CAS registry currently has more than 120 million chemicals and materials known. The 2016 amendment to the 1976 Toxic Substances Control Act (TSCA) brought the number of inventoried compounds to more than 67,600 [10]. On the other hand, it is reasonable to say that there are probably around "only" 10,000 different chemicals commonly use in the chemicals industry. This is not outrageous but when you begin to consider the interactive properties of each of these chemicals – from reactivity to mixture properties – the problem of assessing hazards becomes significant or impossible if relying on tabulated recorded data. An alternative to tabulated data is the use of property estimation methods to predict physical properties as well as hazards associated with green engineering; organism toxicity, fate in the environment, bioconcentration, or bioaccumulation [4]. EPI Suite [11] is an example of a predictive tool provided by the U.S. EPA that uses chemical functional group or structure activity relationship models to predict physical properties as well as empirically derived models that correlate properties like Henry's constant or octanol-water partition with aquatic toxicity, bioaccumulation, biodegradation, environmental persistence, or environmental fate. For certain hazard associated properties, a certain quantifiable number is an adequate representation, but not always. Case in point relates to toxicity where an LC50 or recommended exposure limit can be measured or estimated, but this does not disclose the type of toxicity or information contained in a full dose-response curve. Ultimately, the many tools available to assess hazards can be useful for preliminary design, however, the limitations of each value should be considered.

EXPOSURE: The other half of the risk equation is exposure. Considerations include the route of exposure (inhalation, ingestion, and adsorption), duration (acute versus chronic), and magnitude or amount of the exposure within a period of time. Again, conventional measures can be used to assess exposure within the confines of a chemical plant by understanding the design around chemical storage and transportation, containment safeguards, ventilation, and waste treatment. Furthermore, there are tools available to assess and quantify fugitive emissions based on the plant design and operations [4].

Expanding beyond the conventional to encompass green engineering tools requires adapting fate and transport models into an environmental system. Consider the case of a large-scale accidental release of a known hazardous compound. Exposure assessment will require determination of the fate, which is dictated by the physical properties as well as transport and kinetics. For example, the volatility or Henry's Constant will dictate the relative partitioning between air and water, while the water solubility or octanol-water partition coefficient will dictate the partitioning between the water and soil. The octanol-water partition coefficient can also be predictive of bioaccumulation, plant uptake, or skin/gut/gill absorption.

Environmental transport is also a significant piece of the equation. The environment is a complex system with convective flows of air and water that will distribute the hazardous compound from the original site. Thus, the exposure concentration will be a function of the distance, time, environmental conditions, and partitioning between the air, water, soil, and silt. Degradation kinetics also determine a chemical's fate in the environment. Atmospheric persistence is governed by hydroxyl radical oxidation reactions. Similarly, aquatic degradation is controlled by hydrolysis reactions. In the simplest assessment, kinetic rate equations for different chemical compounds can be estimated in order to estimate the overall biodegradability in the form of an index or environmental half-life. Other methods are available to model the aerobic and anaerobic biodegradation of compounds [4]. Once assembled, it is possible to perform a continuum-based modeling approach to solve a collection of partial differential equations that account for transport and reaction kinetics in order to determine concentrations for any scenario.

Chemical fate and transport in the environment is a complex field of study and a vital component to green engineering [12]. For a more cursory evaluation, a tool such as the EPA's EPI Suite [11] is an excellent option for comparative analysis of different compounds that may be considered for a given chemical synthesis or industrial process. For the case of MA synthesis, it is easy to compare n-butane versus benzene raw material or water versus dibutyl phthalate for the separation. However, another question may be to evaluate an alternative for MA all together or maybe even bioderived routes from renewable succinic acid.

4.3.4 Level 3 Green Chemistry Metrics

The third level of metrics are all-encompassing and extremely rigorous. These include life-cycle assessment (LCA), risk analysis, and sustainability analysis. These tools are equivalent in scope to a conventional full process design evaluation. In-depth discussion of these methods is beyond the scope of this chapter, however, there are many resources available for these topics. As an alternative, we will now focus on one aspect of the chemicals industry that can significantly impact the sustainability of a process: solvent use. We will illustrate how the Principles of Green Engineering can be used to aid in the design and overall sustainability of processes employing solvents across different life-cycle stages.

4.4 Use of Green Solvents in the Chemical Industry

Solvent applications range from product formulation to industrial manufacturing and processing. In consumer and commercial products alone (non-industrial) – the estimated amount of organic solvent usage is over 972,000 tons per year [13]. Including the solvent used for manufacturing across a product's life cycle dramatically increases this number. It has been estimated that solvents can typically account for 80% to 90% of mass utilization for batch processing of pharmaceuticals and fine chemicals [14]. While solvent use in continuous and larger scale bulk chemical production would be reduced, it still has considerable impact on green chemistry and engineering metrics as well as life-cycle impacts for a process [15].

Throughout the chemical processing industry, the use of solvents is commonplace in order to facilitate unit operations and attain product specifications. Solvents have traditionally played a key role in chemical processes for a number of reasons – they may lead to higher quality product, reduce by-product formation, enable product/catalyst separations, reduce the necessary number of process steps, and even be used as a reactant itself [16]. Frequently solvents are used in large excess of solutes and reactants in order to maximize yields. As such, they can greatly contribute to waste production and life-cycle impacts [17]. Calculated E-factors for the production of chemicals have shown that generally the mass of waste is 1 to 5 times the mass of chemical produced for bulk chemicals and, 5 to 50 times for fine chemicals and 25 to 100+ times for pharmaceuticals [15]. Of this waste it was found that upward of 80% may be attributable to solvents [17]. From the engineering perspective, more efficient process design can be implemented to minimize impacts by decreasing solvent requirements and/or maximizing recyclability.

In addition to efficient processing, green design of solvent applications must also consider solvent properties including physicochemical properties, which affect the functionality, acute hazard, and environmental implications associated with solvents. These properties include solubility, polarity, hydrophilicity, and volatility which will affect risk from both a hazard and exposure perspective. These hazards include flammability, explosion risk, and acute toxicity with exposure routes through workplace and consumer contact. These properties also impact environmental implications of solvents associated with fate and transport. As such these properties must be considered across a product life cycle to determine risks to environmental health including greenhouse gas, bioaccumulation, and ecotoxicity metrics [18]. In this context, the principles of green engineering provide guidelines for choosing better solvent alternatives and utilizing solvents more efficiently. The examples below illustrate how the principles can influence solvent design and utilization.

4.4.1 Waste Prevention

One of the best ways to reduce impacts associated with solvent use is to minimize the use of solvent. These reductions can include incorporating solvent-free approaches and/or increasing process efficiency to decrease losses and maximize solvent recycling. Examples of solvent-free reactions in organic reactions, multiple component condensations, and heterocyclic syntheses using catalysts [19] and strategies such as, microwave and ultrasound irradiation [20], eutectic melt [21], and mechanochemistry [22]. It should be noted, however, that while no solvent is added to these systems, that reagents may be hydrated or form compounds such as acetic acid that could have a solvent effect [22]. While solvent-free options are expanding, the utility of solvents for improvements in yields, phase mediation, and separations often cannot be circumvented. Guided process design can aid in making these reactions and separations more efficient. For instance, the use of flow chemistry, microfluidics [23], and reactor design [24] may aid in reaction yields while minimizing ancillary solvent usage.

Given the unavoidable role of solvents for certain applications, judicious solvent choice that weighs hazard, exposure, recyclability, and life-cycle impacts is required. As such, the following principles consider how solvents as well as the systems/processes they are involved in can be designed to minimize their impacts. These principles guide us to choose solvent alternatives that are inherently nonhazardous, have minimal end-of-life impacts, and are renewably sourced. Furthermore, process specific principles address embedded complexity, designing for separation, and process integration for minimization of energy and materials. Examples of both conventional and neoteric solvents help to illustrate trade-offs across the solvent life cycle from sourcing, manufacturing, use, and end-of-life.

4.4.2 Inherently Non-Hazardous

While hundreds of organic solvents are available, water is an obvious choice as it is inherently benign with further advantages in that it is readily abundant and cheap. Aqueous-phase chemistries and extractions are well precedented with water being the choice solvent in biological systems [25]. The use of pure water may be limited by its highly polar behavior as well as its utility with heterogeneous catalysts [26]. These limitations may lead to the use of large volumes of water and/or utilization of surfactants to facilitate compatibility [27]. The recycling or disposal of water typically requires treatment for contaminants; these types of separations processes may be energy intensive particularly for large volumes and may require monitoring to ensure compliance. The use of surface-active agents may facilitate localized high concentrations of reagents within micelles, enabling reactions in an aqueous environment. While low concentrations are typically necessary, surfactant recovery may prove difficult [25]. As such life-cycle impacts of the production and disposal of surfactants must be considered for each application. However, designer surfactants, including bio-derived options, for micellar catalyst-enabled reactions is an growing field that could improve impacts associated with their use [28]. Developing chemistries in water also include the use of enzymes, nature's catalyst for selective and low-impact reactions. High-pressure/temperature and supercritical water has been explored as a powerful solvent for both extractions and reactions [27–29]. At ambient conditions, water acts as a solvent for ionic species, however, at and near supercritical conditions, the polarity shifts and water acts as a non-ionic species solvent. This range may be exploited for a number of different applications ranging from hydrolysis reactions to biomass extractions of non-polar, polar, and ionic compounds [30]. The high critical point of water at 647K and 22 MPa, however, requires significant energy contributes for heating and pressurization and must be considered from an energy use and cost (both capital and operating) perspective before adoption.

Despite advances in solvent-free and water-based solvent applications, organic solvent use is still prevalent and necessary for many reactions and separations processes. Over the last couple of decades, much attention has been paid to finding suitable, less hazardous solvent alternatives, particularly for the high solvent intensity industry of pharmaceuticals. As such, several solvent selection guides have been published through various companies including Sanofi [31], GlaxoSmithKline [32], (GSK) Pfizer [33], and AstraZeneca [34]. These guides use a variety of metrics to attempt to quantify the greenness of solvents for medicinal chemistry applications. The metrics are generally broken up into (process) safety, human health, and environmental categories though GSK has added categories for both waste and life-cycle assessment [35].

Table 4.2 summarizes the main parameters that are considered in the development of the Pfizer, Sanofi, and GSK guides. A common feature of all the guides is to utilize available environmental, health, and safety (EHS)

Table 4.2 Solvent properties to consider for EHS and life-cycle impacts.

	Safety	Human Health	Environment	Waste	Life Cycle
Pfizer	**Process Safety** Flammability (vapor pressure) Explosion risk Electrical Conductivity/Static Charge Peroxide formation potential	**Worker Safety** Carcinogenicity Mutagenicity Reprotoxicity Skin Absorption/ Sensitization Acute Toxicity	Ecotoxicity Water contamination Ozone Depletion Photoreactive Potential		
Sanofi	Flammability (flash & boiling point) Explosion risk (GHS) Autoignition temperature Electrical Conduct./ Static Charge Peroxide formation potential	Carcinogenicity Mutagenicity Reprotoxicity Skin Absorption/ Sensitization Acute Toxicity Boiling Point GSK	Energy demand (boiling point) Aquatic Ecotoxicity Bioaccumulation Ozone depletion		
GSK	**Flammability and Explosion Potential** Vapor Pressure Electrical Conductivity/ Static Charge Boiling Point Flash point Autoignition Temperature **Reactivity and Stability** Peroxide formation potential Explosion risk (NFPA reactivity rating) Self reaction potential Acidity/basicity	**Exposure** Occupational exposure limits **Hazard** GHS risk phrases Carcinogenicity Mutagenicity Reprotoxicity	**Aqueous** Acute and chronic ecotoxicity (GHS) Biodegradation **Air** Photochem O_3 creation potential Vapor Pressure	**Waste score:** Incineration (water solubility, emissions, and enthalpy of combustion) Recycling (ready drying/separation from water, safety aspects) Biotreatment (BOD, VOC potential, K_{ow}) VOC emissions	**LCA score:** Net mass of materials consumed Gross Energy usage Total water consumption Total organic carbon Fossil fuel feedstocks POCP equivalents Greenhouse gas emissions Acidification Eutrophication

data from a variety of sources. For example, many use the Globally Harmonized System (GHS) for health and safety data as a rich source of information for many chemicals including solvents providing EHS data for toxicity and flammability/explosion risks in their safety scores [36]. Complete information, however, may be lacking particularly for newer solvents. Furthermore, information may also be inconsistent between sources and must be verified [37]. Note that while all the guides use many mutual EHS metrics, other metrics, particularly in the environment category are not considered or weighed equally among different rankings. Furthermore, metrics such as boiling point, volatility, and water solubility are physicochemical properties that generally relate to the exposure rather than inherent hazard of the solvent; both of which should be considered for full risk assessment. In utilizing these properties within multiple metrics, their impact becomes incorporated in various metrics and could compound or confound their importance. For instance, in the case of boiling point/vapor pressure, high boiling point solvents have lower risk in terms of air emissions and exposure but the commensurate low vapor pressure means that more energy would be required for distillation for reuse [31]. Further comparisons of these solvent guides can be found published elsewhere [18, 35, 38].

The importance of the chemicals industry for sustainability is reflected in REACH, recent regulation in the EU that was "adopted to improve the protection of human health and the environment from the risks that can be posed by chemicals, while enhancing the competitiveness of the EU chemicals industry [39]." Motivated by REACH, AstraZeneca has recently formulated a guide that includes 272 different chemicals [34]. The framework surveys physical parameters (e.g., boiling point, density, refractive index), solubility parameters, chemical properties (e.g., flash point, water solubility) of the solvents, though comprehensive data for all solvents is not available. Their works seeks to provide a prediction tool for determining best alternatives using principal component analysis and potentially providing unconventional solvent solutions. While these guides provide a number of alternatives to current solvents, there are not always drop-in replacements that are readily available. For example, the AstraZeneca guide highlights the lack of ready alternatives for dipolar aprotic solvents such as N,N-dimethylformamide (DMF), N,N-dimethylacetamide (DMA) [34]. Furthermore, these alternatives typically still have significant life-cycle impacts and as such only provide a step toward sustainable processing. As such neoteric alternatives are being developed that are high functioning but also minimize impacts according to the principles of green engineering. Ranging from bio-based solvents to ionic liquids and carbon dioxide, the hazards associated with these neoteric alternatives must still be carefully considered across the process life cycle.

4.4.3 Renewable Rather Than Depleting

Biomass-derived solvents stem from a variety of feedstocks from lignocellulosics to oleaginous materials [40]. As such they may span a large range of necessary solvent properties [35, 41]. Glycerol is a particularly interesting feedstock as it is a co-product of biodiesel production that has low value and has even been ascribed as waste. The valorization of glycerol as a solvent and/or derivatization to produce other solvents or chemicals adds economic incentive and can decrease environmental impacts associated with the production of biodiesel [42]. While there is much potential for renewably based solvents, not all bio-derived solvents are in fact non-hazardous [40]. EHS metrics should be evaluated to make sure that these solvents are inherently benign. Furthermore, life-cycle metrics can be used to analyze their potential impacts including all stages such as production and end of life. Several studies have looked at the potential impacts of some of these bio-based solvents indicating that like petroleum-derived solvents, they also have the potential to have significant toxicity and are potentially not biodegradable. For example, in the production of hexamethylenediamine, several routes were evaluated via life-cycle assessment in order to compare bio-based versus fossil-based methods for manufacturing. The study found the fossil-based route to be more economical and with generally lower life-cycle impacts than the bio-based alternatives [43]. The study found trade-offs for certain alternatives between life-cycle metrics particularly related with eutrophication impacts due to the use of fertilizers. This trade-off is often associated with bio-based products and could be potentially mitigated by more effective nutrient application or more complete bio-based feedstock utilization allowing for a spread allocation of impacts across a number of products [44].

In addition to conventional techniques, advancements in computational strategies have recently been used for new solvent development. *In silico* design strategies can be used to generate feasible molecular candidates from renewably based building blocks and predict their functional properties. This powerful technique can reduce time and waste during solvent development including selecting from a potentially large spectrum of candidates. These method may be particularly valuable for certain solvent categories (e.g., polar aprotic, asymmetric halogenated hydrocarbons) where no or few good alternatives exist [45]. For example, the dissolution of nitrocellulose was evaluated for potential green solvent alternatives to conventional solvents like butyl acetate, xylene, and toluene, all of which are flammable and pose other safety risks. Using this *in silico* approach, diacetin, a glycerol-derived compound, was isolated as a strong candidate with low EHS impacts. Computation approaches can certainly aid in the effort to establish solvent alternatives. Unfortunately, for many of these compounds, only empirical data for all parameters is available and thus estimates are used for physicochemical properties and life-cycle impacts – development of this type of data would enable more accurate and models and better alternatives to be established.

4.4.4 Design for Commercial After-Life

The fate of solvents after their direct use may have significant weight on their life-cycle impacts and must be evaluated with regards to a number of metrics (Table 4.2). While dozens of possible metrics could be used (from eutrophication to ozone depletion or emissions potentials) certain key metrics are distinctly important given specific applications. For example, the feedstock/materials extraction phase is particularly important for bio-derived products since the use of fertilizers and water can lead to high eutrophication potential and water use.

To some extent, the environmental fate and transport of solvents can be estimated via physicochemical properties of the compounds themselves [46]. High volatility/low boiling point solvents are more likely to partition to air. Partitioning can also be determined by such correlations as Henry's law or the octanol-water partition coefficient which may be used to estimate water/air partitioning, bioaccumulation, and to some extent soil sorption. The compartmentalization of these compounds will also determine the potential exposures for such end-point impacts as aquatic ecotoxicity and biodegradability.

Despite the importance of determining end-of-life impacts, taking all of these joint factors into account is difficult and the weighting between each of the impacts elucidates trade-offs that should be considered during solvent selection. As such, environmental impacts are the most varied set of parameters evaluated among the solvent selection guides (Table 4.2). All account for ecotoxicity and ozone depletion by some means, though the accounting for other metrics vary. In the case of Sanofi, the major environmental assessment is done via boiling point correlation where high boiling point components are penalized as they require high energy for recycle. This phenomenon is also noted in the GSK guide [32]. This approach, while limited also starts to address some of the life-cycle impacts that would need to be addressed for solvent reuse. Previous researchers have recommended the avoidance of distillation as a separation technique in order to cut down on life-cycle impacts associated with the high energy use [46]. The GSK guide is the only one that extensively accounts for life-cycle impacts in its guide [32].

4.4.5 Separation and Purification to Minimize Energy Consumption and Materials Use

Separations are particularly energy intensive operations. It has been estimated that separations processes can consume up to 40% of energy use in chemicals manufacturing and may contribute to more than 50% of operating costs [47]. Distillation is the most prevalent industrial separation process and represents a large portion of process energy. As such, in the search for green solvents, one criteria often considered is the vapor pressure/boiling point [46]. A low boiling point requires less energy for solvent distillation, however, the commensurate high-vapor pressure has potential ramifications for inhalation exposure and atmospheric life-cycle endpoints. Current focus on novel means for separation include membranes, crystallization, and chromatography, however, these processes still require significant improvements in order to decrease energy consumption and make them cost-competitive to distillation.

Switchable solvents are a promising solvent alternative that are designed for ready separation. These solvents contain a property that is easily flipped given an external trigger. For example, some switchable solvents can flip polarity or hydrophilicity using CO_2 as the switch [48]. The change in property can be useful for both reactions (drawing products into separate phases) and extractions. For example, a switchable hydrophilicity solvent was used for soybean oil extraction. Typically, this type of oil extraction is done with hexane which has toxicological consequences and requires distillation. Using a switchable solvent in the hydrophilic form, oil is first extracted from soy bean flakes. Water is then added to separate the solvent and oil. In order to recover the solvent, CO_2 is then sparged through the water/solvent mixture to switch the solvent to the hydrophobic form and recover the solvent which can then be switched back to its original hydrophilic form [49]. While these applications are promising, the use of SHS is not currently commercially represented, however, design of these solvents for particular applications with further improvements in recovery and yields could aid in the adoption of these solvents for alternative separations [50].

From a separations perspective, another interesting green solvent candidate is high-pressure carbon dioxide either in liquid or supercritical states. CO_2 has been used for extractions, reaction mediation, and chromatography. One major advantage is that its properties are potentially tunable with varying pressure and temperature as well as the use of co-solvents [51]. The use of pure CO_2 for extractions is growing in popularity for food applications as this solvent is completely non-toxic and can easily be removed by bringing the pressure down to ambient conditions [52]. The use of co-solvents such as methanol or ethanol extends the solubility range of CO_2. Adding a secondary solvent does potentially require downstream separations, however, these co-solvents are used in much smaller quantities than conventional solvent operations thus decreasing separations burdens. Despite the promise and prevalence of research applications using CO_2 few have come to commercial fruition. Common reasons for this include risk aversion due to high capital costs and operating costs associated with the energy input needed for CO_2 compression during pressure swings needed for product recovery. However, recent studies have shown that pressurization is not the most energy-intensive step for CO_2 extraction (chilling and heating also play a significant role) but that total energy is comparable to that of distillation processes [53]. New methods that may improve the energy use of CO_2 extractions include improving recyclability without large changes in pressure (e.g., using membranes or adsorption) and process integration.

4.4.6 Integration and Interconnectivity with Available Energy and Materials Flows

Throughout a process, solvents are integrated into numerous unit operations where the integration of energy and materials flows would enable gains in efficiency. In the previous example, using supercritical CO_2, heat integration could significantly reduce the energy needed for heating and chilling of the supplied CO_2. Since the critical temperature of CO_2 is 304K, operating temperatures could be supplied by waste heat. Integrated process flows could also be used for switchable solvents where waste CO_2 produced from various processes could be used in a switchable solvent system [48]. Another notable example of process integration is reactive distillation where products are being separated as they are formed, creating a better driving force for better yields and higher purities [54].

The possibility of mass/energy integration with respect to both conventional and neoteric solvents could be evaluated circumstantially. For instance, the use of solvents in an integrated biorefinery would ideally produce a number of different products while utilizing selective solvents that could produce a variety of products [35]. Specifically, during the production of biodiesel the process includes a reactor and several distillation columns to remove product from by-product (glycerol) and excess methanol for recycle. It was shown that by integrating heat exchangers and water flows from distillation columns and reactors in various biodiesel production scenarios, that the energy and water consumption was significantly decreased for production [55]. This example provides insights into how appropriate process design could aid in the more sustainable use and recycling of system components including solvents.

4.4.7 Conserve Complexity

Minimizing the complexity of a process from the original design could help to circumvent unnecessary losses. As such decreasing the complexity of components used as well as the number of process steps required could aid to minimize process impacts. From the perspective of solvents this may refer to the number of steps needed

Table 4.3 Life-cycle considerations for green engineering with solvents.

Raw materials sourcing	Production	Utilization	Recycling/ Disposal
Fossil versus biobased	Synthesis steps	Exposure to workers and consumers	Distillation/separations
Renewable versus depleting	Intermediate exposures	Functionality	Disposal method
Accessibility	Energy and resource consumption	Separations	End-of-life impacts (biodeg., ecotox., etc.)

to produce the solvent itself or those needed for the use/re-use of the solvent. Ionic liquids (IL) serve as a prime example of embedded complexity in the production of solvents. Often considered green solvents due to their low vapor pressure (minimizing inhalation exposure and facilitating product distillation), the actual impacts of IL are sometimes called to question due to their potentially high toxicity [56] and large number of synthesis steps [46, 57].

With regards to ionic liquids, the evaluation of these potential solvents touches many aspects of green engineering, highlighting many of the previously mentioned principles. A life-cycle analysis comparing the use of IL ([Bmim][BF_4]) to conventional solvents for two reactions showed that conventional methods had better or comparable life-cycle impacts to the IL [57]. While these results indicated that the evaluated IL was not the most attractive alternative, it also highlights where improvements to IL separation efficiency and recyclability would improve the life-cycle outcome. As such, recent attention has been paid to the production of lower impact IL. For example, renewable/readily available materials have been used for production of IL [58] using low-impact syntheses. Furthermore, many IL have traditionally shown high human and ecotoxicity; however, several new IL are being developed from biological materials enabling their use for food applications and reducing the hazard from exposure to humans or environment [59]. Highly recyclable IL with low cost are also being developed [60]. The recyclability has a strong impact on the cost; for example, a technoeconomic analysis showed that even for a high recycle rate of 99.6%, IL costs are estimated at 39% of the minimum ethanol selling price [61]. Other advances in the field of IL include developing tunable formulations depending on the anion and cation identity. Tunability could lead to better selectivity and efficiency, thus allowing for lower impacts [62].

As the previous examples have highlighted, there is much opportunity in the field of solvents to find and implement greener alternatives. These solvents must be evaluated across the entire life cycle from sourcing to disposal of the solvent in terms of an array of indicators that can be categorized into environmental, efficiency, economic, and energy endpoints [63]. Table 4.3 highlights factors to be considered at each life-cycle stage with respect to the design and use of green solvents. As a consequence of innovations in this field, there have been several Presidential Green Chemistry Awards that have been awarded to applications specific to solvents from water to CO_2 and will be discussed below.

4.5 Presidential Green Chemistry Awards

To find examples of 12 Principles of Green Chemistry and Green Engineering being employed in research and on an industrially relevant scale, one most look no further than the winners of the Presidential Green Chemistry Challenge Awards, established in 1996. As of 2016, it is estimated that the award-winning technologies have eliminated 826 million pounds of hazardous chemicals each year, saved 21 billion gallons of water each year, and eliminated 7.8 billion pounds of CO_2 equivalents each year [3]. In each award-winning technology, the 12 Principles of Green Chemistry and Green Engineering are evident, green chemistry metrics are used to demonstrate the magnitude of the advantages, and undoubtedly, every adopted technology was also economically beneficial. Here are a few examples of award-winning technology focus on green solvent usage.

In 2011, Bruce Lipshutz received the academic award for the use of water as a solvent using surfactants in order to allow for chemical reactions in water and circumventing the need for production of organic solvents. While the surfactants still need to be produced, the quantities are much smaller than those of organic solvents.

Eastman Chemical won the Greener Synthetic Pathways award in 2009 for creating a solvent-free enzymatic production of esters for their cosmetic and personal care products. Purportedly the process can save over 10 liters of organic solvent per kilogram of product and has benefits in terms of product purity, cost, and life-cycle impacts.

The 2006 Small Business award was given to Arkon Consultants and NuPro Technologies, Inc., for their work on the development of a system that reduces solvent use and replaces solvents with greener alternatives. As a result, the system reduces explosion potential and emissions during solvent recycling. Typically, in flexographic printing, a mixture of chloro-saturated cyclic, or acyclic hydrocarbons (such as xylene) are used for washing of their printing plates. Firstly, new solvents were developed using bio-based solvents which also improved EHS properties (flash point, toxicity, explosion potential, workplace exposure) for their solvents. They also developed a recycling system using filtration and centrifugation to lower workplace exposure to the solvents as well as improve recycling.

The 2004 Academic award was given to Professors Charles Eckert and Charlie Liotta for their work combining reactions and separations in tunable solvent systems. Using both CO_2 and water, they have provided a body of work that takes advantage of the differential properties of high pressure systems, tuning the conditions for optimal reaction and separations conditions including the use of phase-transfer catalysts. These techniques also allow for improved catalyst recycling and have been used for a variety of applications in the chemical and pharmaceuticals industries.

The 1998 Green Reaction Conditions award was given to Argonne National Laboratory for their synthesis of lactate esters, sugar-derived solvents, for the replacement of more hazardous solvents such as halogenated constituents. The award is for their membrane reaction/separation process that uses pervaporation membranes and catalysts for the liquid and vapor product separations that allows for ammonia separation and utilization from the other reaction constituents acids/esters/alcohols. The process was able to decrease waste production while making the production of this renewable solvent more economical.

4.6 Opportunities and Outlook

In closing, the opportunities for green engineering innovations in the chemicals industry are many and the outlook is bright. There are numerous metrics-based tools for evaluating how green a process or product is, and in many cases the difficulty is determining the best set of metrics and evaluating the entire picture. There is significant opportunity for innovation in this field, particularly as our natural resources continue to be depleted, global population is growing, societies are advancing, and the global environmental burden increases. Green engineering is a key aspect of sustainability and must be at the forefront of our minds as we design new process, build new plants, and revolutionize our industry.

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5

Process Intensification in the Chemical Industry: A Review

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5.1 Introduction

It is difficult to give an appropriate and exact definition of the term “Process Intensification” (PI). Often, process intensification is associated with attractive but vague expressions like “cheaper, smaller, cleaner” or “making more with less”. However, all these purely descriptive and qualitative attributes do not contribute to defining the term “process intensification” in a rigorous way. The problem with the PI definition is actually related to the identification of the limit (if any), which allows discrimination between real process intensification and classical process optimization. Generally speaking, PI technologies tend to completely re-design conventional unit operations and, also, make use of novel equipment or processing methods such as multifunctional reactors, micro reactors, enhanced heat exchangers, alternative energy forms, and so on. The recent developments in both climate change and energy supply have confirmed the necessity of faster and wider application of innovative PI-technologies, which can offer significant advantages like decrease of capital and operating expenses, selectivity improvements, lead time reduction and safety improvement.

In recent years, the development and the exploitation of PI methods has seen a worldwide hastening. Starting from the mid-1980s, the interest of both academia and industry in process intensification increased to a significant extent, as testified by the number of articles published in this field. A literature search performed by *Web of Science*, considering

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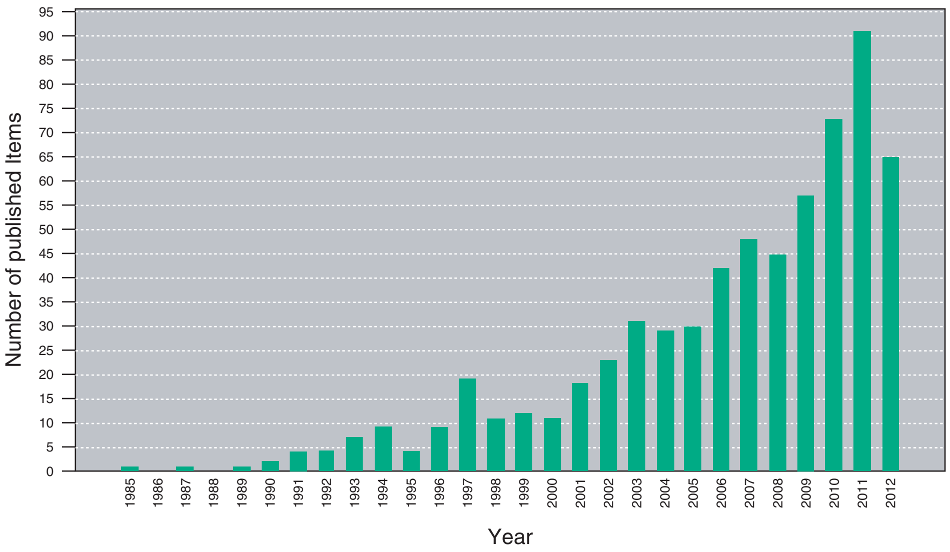

Figure 5.1 *Number of published papers – keywords: "Chemical" AND "Process Intensification". Data collated from www.webofknowledge.com*

the words "chemical" AND "process intensification" returned the result shown in Fig. 5.1: the number of publications in the last few years seems to stabilize in the range 45–90 papers per year, with a peak in 2011. In addition, it is worthwhile remarking that a scientific journal, namely *Chemical Engineering and Processing: Process Intensification*, focuses on PI and on different related fields.

Another fundamental reference in PI field is represented by the European Roadmap for Process Intensification, which presents a valuable review of PI technologies analyzed from an industrial standpoint.

5.2 Different Approaches to Process Intensification

PI methodologies have been extensively applied to improve the performance of several chemical processes. PI has the potential to positively affect a process by increasing its efficiency via a reduction in energy consumption, costs, volumes handled, waste generated, and, by improving the process safety without sacrificing product quality (Reay *et al*., 2008). Retrofit is a fundamental concept in PI and can be defined as the improvement of an existing plant by substituting or improving some of its constituent unit operations while fitting the rest of the plant and some of the process variables, namely the chemicals processed by the system, the reactions that may be occurring, the product purities that need to be achieved, a sub-set of equipment and operations in the process (Lutzea *et al*., 2010). Actually, a proper discrimination between drastic improvements and improvements as just a result of qualitative changes has to be done. Microreaction technology, monolithic reactors and reactive separations are classical examples of a drastic enhancement, since they allow, as compared to traditional apparatuses, improved mass and heat transfer rates, thus achieving significant improvements as compared to traditional technologies. Alternative forms of energy supply for chemical reactions such as microwaves and ultrasound, the use of new reaction media such as ionic liquids, micro-emulsions and supercritical phases, or the use of new auxiliary agents such as phase transfer catalysts belong, instead, to the second category, even if they are also capable of improving the existing processes. The principles associated with PI have been classified (Lutzea *et al.*, 2010) considering three different kinds of enhancements, which can be achieved through: (1) the integration of operations; (2) the integration of functions; and (3) the integration of phenomena. In this way, PI is accomplished by adding and enhancing a phenomenon within a function and/or operation for improved equipment design in order to maximize the driving force or to overcome the limitations occurring in the corresponding conventional process. In addition to these three principles, a targeted enhancement of a phenomenon can be considered as well; in this way, PI is achieved through improved use of the respective phenomena/functions to overcome the limitations occurring in a given conventional operation. Van Gerven and Stankiewicz (2009) defined four principles to achieve a completely intensified process: (1) to maximize the effectiveness of intra-and intermolecular events; (2) to optimize the driving forces at every scale and maximize the specific surface area to which these forces apply; (3) to maximize synergistic effects; (4) and to give each molecule the same processing experience. Finally, another possibility for the classification of process intensification measures is to divide them into three superordinate levels (Freund and Sundmacher, 2008). The most detailed level is the so-called *phase level*, at which molecule populations, which build up a thermodynamic phase, are considered. In a whole process, all the thermodynamic phases are embedded into apparatuses, or into individual process spaces. This is the so-called *process unit level*. Usually, the process consists of several such process units. The interconnection between the individual apparatuses and thus the overall process flowsheet can finally be analyzed at the superordinated *plant level*.

5.3 Process Intensification as a Valuable Tool for the Chemical Industry

From an industrial standpoint, PI has been successfully exploited in many different sectors, as discussed in the European Roadmap for Process Intensification.

In petrochemical industry, for instance, energy definitely represents a relevant part of total delivered product costs. Energy efficiency significantly affects the cost competitiveness and sustainability of petrochemical industry, which, in recent years, has already attained considerable improvements in energy efficiency. Given the large size of the petrochemical industry and the highly competitive market in which it operates, it is worthwhile combining reliability and predictability in order to achieve a decrease in energy expenses. Unexpected production interruptions do indeed have serious impacts on operational and logistic costs and may easily erode profits. In this context, PI may play an important role either in reducing energy costs or in lowering capital needs for investments, keeping safety and process reliability at the levels required by both legislation and market. PI does indeed aim at promoting innovation, creating technology breakthroughs for any industrial sector and, therefore, also for petrochemical industry processes (Harmsen, 2010). As far as energy efficiency is concerned, it is expected that the exploitation of process intensification methodologies may determine at least a 20% improvement by 2050 (Sanders *et al.*, 2012). This will be achieved by implementing new technologies, for example, new processes, bio-based and bio-catalytic routes, novel materials, hybrid reactors, novel separation systems, and so on. Like all new technologies, however, PI faces several barriers, which need to be overcome to effect an efficient PI implementation. These barriers can be summarized as: high cost to retrofit PI technologies in current production processes; risks of commercializing breakthrough technology; scale-up of PI; lack of PI knowledge, unfamiliarity with PI technologies and, finally, a long development path (Ren, 2009).

In the pharmaceutical/fine chemicals industry the use of process intensification methods is called to increase the selectivity of reactions (Yadav *et al.*, 2003) and, thus, the material yield, reducing the lead time (i.e., the time between raw materials delivery and the completion of the product) of the entire production process. The achievement of these goals would also determine savings in energy consumption and contribute to related sustainability needs. Currently, the typical selectivity of chemical reactions is about 80%; PI technologies can increase selectivity up to 90%. For a classic multi-step process, this would achieve a rise in material yield from 30–60%, which significantly contributes to the sustainability of the whole process. Moreover, current processes in the fine chemicals industry may have up to 50 process steps, with a lead time of several months. The exploitation of improved design methods based on PI will allow operating integrated and continuous process steps, thus reducing these lead times to a significant extent. It is indeed expected that a multipurpose serial production train, based on PI technologies, can result in 50% reduction of production costs within 10–15 years. However, this vision can be achieved if PI technologies, whose efficiency has been proved on lab-scale plants only, are properly scaled-up and industrialized. However, a successfully implementation of PI technologies in the pharmaceutical/fine chemicals industry is actually dependent on a detailed insight, at molecular level, of both kinetics and thermodynamics of the reactions participating in the process (Gernaey *et al.*, 2012). This knowledge is essential to formulate reliable models, which are called to predict the influence of process and operating variables on system behavior. A dependable model is indeed necessary for the implementation of a proper control system since it allows investigating how the process outputs may change with time under the influence of changes of the external disturbances and manipulated variables. Another important factor that has to be accounted for regards the development of effective on-line analytic techniques aimed at monitoring and validating the “intensified” continuous processes. Also in this case, PI faces several barriers (Lutzea *et al.*, 2010): suppliers for industrial applications of PI technologies are lacking; the design of novel PI apparatuses on pilot-/industrial scale is expensive and technologically uncertain; the capital cost of novel PI modules per production capacity today is often higher than that of traditional reactors. In addition, efficient solutions for downstream processing in combination with PI reactors where the production of multiple products is combined in a single unit, are difficult to implement.

Agro-food industry is characterized by huge volumes or great flow rates of (very) diluted streams. Cost competitiveness of agro-food industry is significantly affected by two factors, namely the energy costs for processing and the wastes treatment cost.

Both these costs can be reduced exploiting process intensification methodologies (Doré *et al*., 2011) provided that an optimization, performed over the whole agro chain and considering – at least – crop harvesting, transportation, preliminary processing, refining, derivatization process, has been preliminarily implemented. The production chain and processing of agro-food industry is indeed constrained by the limited stability of crops and derived materials. PI can potentially achieve different kinds of optimization. Typical examples are: separation in (or close to) the field of certain crop components determines significant energy and transportation cost savings; preservation of crop components right after harvesting reduces the seasonality effect, leading to much higher capacity utilization of process equipment and related capital costs; valorization of non-foodstuff competitive crop components into the so-called second-generation bio-fuels can be achieved through the exploitation of new crops (waste oils, lignocellulosic materials, whey, etc.) (Sansonetti *et al*., 2009; De Paola *et al*., 2009) and novel harvesting technologies. For instance, using a PI standpoint, milk separation into water, proteins and fats can be performed on-site (i.e., at the farm) with low energy-consuming micro separators. In this way, product transportation to and handling at the factory can be limited to the relevant components, proteins and fats, saving energy and reducing CO_2 emissions by avoiding the unnecessary transportation of water. Different factors have to be analyzed before implementing PI technology in the agro-food industry: crops with short storage limits such as milk, fruit juices, sugar beets, and vegetables do indeed determine particular problems; final product quality is strongly affected by the variability of the agro material due to source and seasonality; finally, the significant increase of crops dedicated for bio-ethanol and bio-diesel production is determining a competition for valuable lands utilization, thus determining the necessity of both intensified crops and novel process approaches. Food industry performance is also affected by market conditions, which request accurate cost awareness that directly turn into technology improvements so as to achieve higher yields. Product quality and food safety are definitely essential issues, which need to be accounted for in relation to consumer and legislation requirements. Food companies, therefore, need updated product innovation in order to satisfy consumer trends and changing demand. In addition, energy efficiency increases, plant safety, and flexibility are considered as important factors, which may contribute to the implementation of proper PI methodologies. Different technologies, having a potential high impact on food technology, have been actually identified. In particular, it is expected that PI will lead to an overall energy efficiency increase of 30–40% by using: (1) milder processing techniques which will result also in a better product quality; (2) more selective treatment of raw materials and ingredients; (3) more effective removal of micro traces of selected compounds; (4) increased processing flexibility (Ammar *et al*., 2012). Moreover, it is expected that a decrease of (bio)-fouling in processing equipment and an increase in cleaning efficiency will determine a 20% capacity growth and a 60% energy saving. An important barrier to PI development in the agro-food industry is the limited availability of true process experts who, generally, concentrate on optimizing the existing plants and pay little attention to new, green, improved processes. This is partially to be ascribed to the fact that novel PI-based technologies are difficult to be incorporated in existing and well-established factories. Food industry is indeed a rather traditional sector not prone to adopting new technologies based, in particular, on PI methods (Fitzpatrick and Ahrné, 2005).

5.4 PI Exploitation in the Chemical Industry

In this section, a description of some process units designed on the basis of PI concepts will be presented, pointing out on their major features, on the advantages determined by the exploitation of these PI units and, in some cases, on the existing barriers that are currently limiting their spread on an industrial scale. Many of these units have already replaced the traditional apparatuses and improved the performance of conventional processes; some others are at a development stage, but it is expected that they may replace the traditional units in the future, hopefully in the next 10–15 years. The following critical review on each of the considered apparatus was readapted from the European Roadmap for Process Intensification where more detailed information can be found.

5.4.1 Structured Packing for Mass Transfer

Structured packing is used in various mass-transfer operations, including distillation, liquid/liquid mixing, absorption, and extraction. It offers high interfacial mass transfer areas and good phase dispersion resulting in high number of transfer units. Many different designs of structured packing are available; most of them are realized in order to form an open honeycomb structure with inclined flow channels and a relatively high exposed surface area (Bessoua *et al.*, 2010).

5.4.2 Static Mixers

Static mixers are pipe inserts which generate radial mixing or, for multiphase systems, produce fine bubbles or droplets (Lobry *et al.*, 2011). Static mixers are particularly useful for the continuous processing of chemicals; their main limitation is sensitivity to clogging. Compared to conventional mixing systems they are characterized by a very high-energy dissipation rate, resulting in very compact and energy efficient units.

5.4.3 Catalytic Foam Reactors

Solid foam catalytic reactors use a solid foam structure as the support for depositing a catalyst. These materials combine high void fraction and high surface area. Catalytic foam reactors (Palma *et al.*, 2012) represent a valid alternative to fixed bed reactors, since they are characterized by lower pressure drop and, hence, lower energy consumption; in addition, in the case of metallic foams, heat transfer is enhanced and more equal temperature profiles are obtained. The major disadvantages are represented by the inherently higher costs of the foam-based catalyst and by the relatively low surface area for deposition of the catalytic material. This technology is still in an early stage of development.

5.4.4 Monolithic Reactors

Monolithic catalysts are made of ceramic materials or corrugated metal sheets and consist of a many narrow parallel channels whose walls are used for catalyst deposition. Monoliths are characterized by narrower residence time distribution, which corresponds, as compared to conventional units, to higher selectivity, higher specific geometric areas, lower mass transfer resistances and, hence, smaller reactor volume, very low pressure drops and therefore, lower energy requirement (Edvinsson and Cybulski, 1994). Monolithic reactors are used in gas-phase cleaning in environmental applications; however, a cost reduction of monoliths and the exploitation of novel materials allowing higher catalyst loading are both required to achieve a wider spread of this technology.

5.4.5 Microchannel Reactors

Microreactors are chemical reactors of extremely small dimensions and usually a sandwich-like structure, consisting of a number of layers constituted by micromachined channels whose diameter may range between 20–400 μm (Fig. 5.2). Microreactors allow very high heat transfer rates (Regatte and Kaisare, 2011), not attainable by other apparatus. Very low reaction-volume-to-surface-area ratios make microreactors attractive for reactions involving poisonous or explosive reactants. Compared to traditional reactors, heat dissipation in microreactors is significantly enhanced by passing the reaction fluid through very small channels, realized in high thermally conductive metal blocks which, depending on the endothermic or exothermic nature of the reaction, are heated or cooled, respectively. The major advantage of microreactors is definitely represented by the excellent control of reaction temperature (Kockmann *et al.*, 2011). The main drawbacks, instead, are high pressure drops, relevant clogging tendency, and high unit cost. Microreactors may be successfully exploited in both fine chemistry and the pharmaceutical industry.

5.4.6 Non-Selective Membrane Reactors

In a reactor equipped with a non-selective membrane, the membrane is used to provide a support for the deposition of a catalyst (Shuit and Ong, 2012; Basile *et al.*, this book).

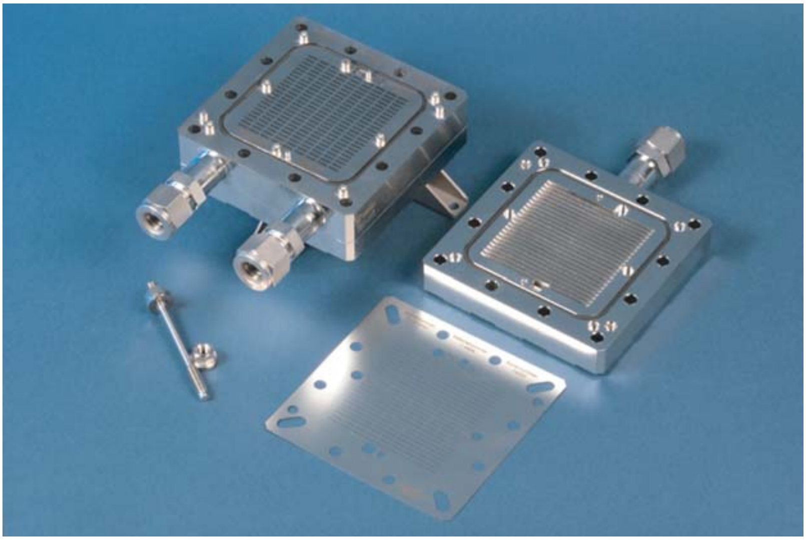

Figure 5.2 *Microchannel reactor. Reproduced from www.vinci-technologies.com*

The reaction, therefore, can take place either inside the pores of the membrane or on its external surface; the membrane is aimed at offering a very effective contact between reactants and catalyst, thus resulting in a short contact time catalytic reactor. An attractive exploitation of non-selective membrane reactor is the controlled dosing of one reactant along the length of the reactor (Rahimpour, 2009), which allows avoiding high local concentrations. The problems that need to be solved for a complete utilization of membrane technology on industrial scale are still represented by the system costs and the membrane stability.

5.4.7 Adsorptive Distillation

Adsorptive distillation is a three-phase mass transfer operation performed in two columns (Mujiburohman *et al.*, 2006); the first one is used to achieve the actual separation, the second one to attain the adsorbent regeneration. The adsorbent is a fine powder, which is fluidized and circulated by an inert carrier. Adsorptive distillation is capable of enhancing separation efficiency, especially in the case of azeotropes or close-boiling components and can be exploited, especially in the fine chemical industry, to perform continuous processes. One significant improvement of this operation is actually represented by the suspension absorptive distillation, where the solid absorptive material acts as an extractant. This technology, however, is still in a very early stage of development and no demonstration of its feasibility or of the actual advantages over traditional alternatives has been yet provided.

5.4.8 Heat-Integrated Distillation

As compared to a classic distillation column, a dividing wall column is capable of delivering pure side fractions, thus reducing the number of necessary distillation columns in a separation sequence. A dividing wall column represents an example of Heat-Integrated Distillation Columns (Kiss and Suszwalak, 2012; Markowski *et al.*, 2007) where the integration is achieved by the combination of the rectifying and the stripping columns in a single arrangement. Dividing wall columns have been effectively used in several chemical processes and can be considered to be a mature technology, which allows, in terms of energy and investment costs, savings even higher than 30%.

5.4.9 Membrane Absorption/Stripping

Membrane absorption occurs when a gaseous component is selectively transported through a membrane and, then, dissolved in an absorbing liquid (Fig. 5.3). One of the most important uses of membrane absorption is represented by CO_2 capture from flue gas (Feron and Jansen, 1997; Belaissaoui *et al.*, 2012). A natural extension of membrane adsorption is represented by either the membrane-based absorption-desorption process, where two liquids are on both sides of the membrane, or the membrane stripping process, in which selected components are removed from the liquid phase through the membrane by a stripping gas. Membrane absorption is actually a bubble-free gas-liquid mass transfer unit operation, which presents several advantages in the case, for instance, of shear-sensitive biological systems.

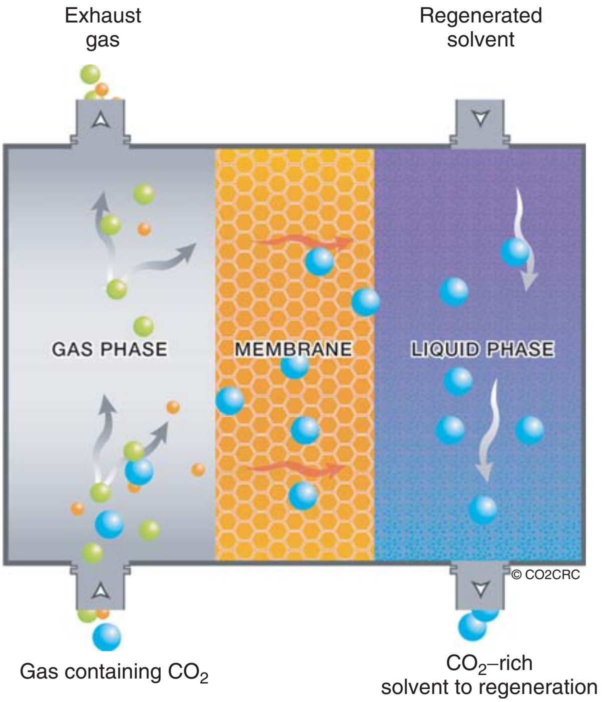

Figure 5.3 *Membrane absorption schematic. Reproduced with permission. Copyright © CO2CRC 2011*

5.4.10 Membrane Distillation

Membrane distillation (Calabrò *et al.*, 1994) is a thermally driven unit operation consisting in transporting a volatile component of a liquid feed stream, as a vapor, through a porous membrane; the vapor is then condensed on the other side of the membrane (Fig. 5.4). This technology offers the potential of performing very efficient separations; however, energy (actually a lower amount as compared to conventional

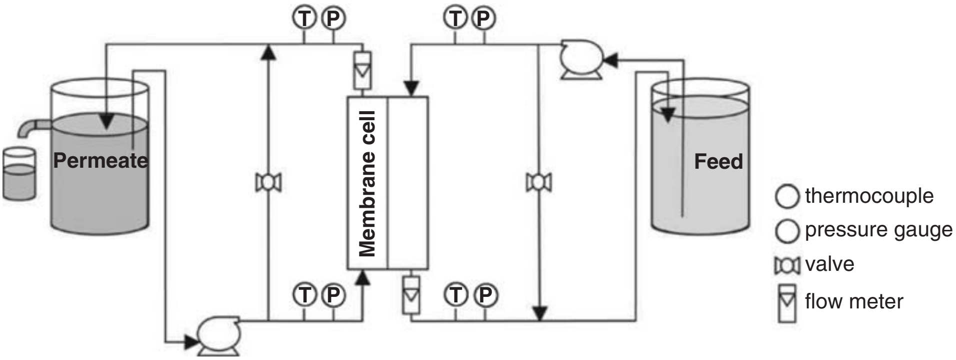

Figure 5.4 *Membrane distillation schematic. Reproduced from www.omicsonline.org*

distillation) is needed for vaporization. Another advantage is represented by the absence of concentration polarization, which, instead, afflicts other membrane operations.

5.4.11 Membrane Crystallization

Membrane crystallization is a novel crystallization technique, used – for instance – for protein crystals growing with enhanced crystallization kinetics. Membrane crystallization allows obtaining better crystal forms under operating conditions that are unsuitable for conventional crystallization processes. This technology is actually given as the combination of crystallization and membrane distillation (Di Profio *et al.*, 2010) and is based on a rather simple principle: the solvent evaporates (by steam/vacuum) at the membrane interface, migrates through the pores of the membrane and eventually condenses on the opposite side of the membrane. The membrane is capable to activate heterogeneous nucleation starting at low super saturation, thus enhancing the kinetics of crystallization, even for large molecules, like proteins (Di Profio *et al.*, 2006). Since all solvent must be evaporated, the process can be rather energy-intensive, even if it operates at a low temperature-difference as compared to the established technology, thus potentially resulting in energy savings. Moreover, due to the lower temperature differences, the crystallization process is carried out at milder conditions and in a more controlled way, which could be of great interest for the pharmaceutical industry.

5.4.12 Distillation-Pervaporation

A pervaporation membrane can be coupled with a conventional distillation column, thus resulting in a hybrid membrane/distillation process (Naidu and Malik, 2011), where the membrane can be placed either on the overhead vapor or on the feed of distillation column. Examples of potential improvements of this technology as compared to conventional processes are breaking an azeotrope, without the addition of a solvent, increasing the capacity of a distillation column and improving quality of the bottom and overhead products. The potential of the technology has been already proved in the case of alcohols dehydration and of the separation of isomeric hydrocarbons.

5.4.13 Membrane Reactors

Membrane reactors represent a very effective system in equilibrium limited reactions, since the products are continuously and selectively removed, thus favoring the forward reaction according to Le Chatelier’s principle (Gallucci *et al.*, 2008). Two well-known examples of membrane reactors consist in hydrogen conducting membranes, based on palladium (Basile *et al.*, 2008), and oxygen conducting membranes, based on perovskites (Evdou *et al.*, 2008). A very wide range of principles and characteristics are actually known; this leads to a broad range of operating conditions that can be used to operate a membrane reactor. Figure 5.5 shows a palladium membrane reactor for the direct synthesis of phenols from benzene.

5.4.14 Heat Exchanger Reactors

In a heat exchanger reactor (Anxionnaz *et al.*, 2008, Despènes *et al.*, 2012) the reaction occurs close to a heat exchange surface, which is aimed at removing (or supplying for

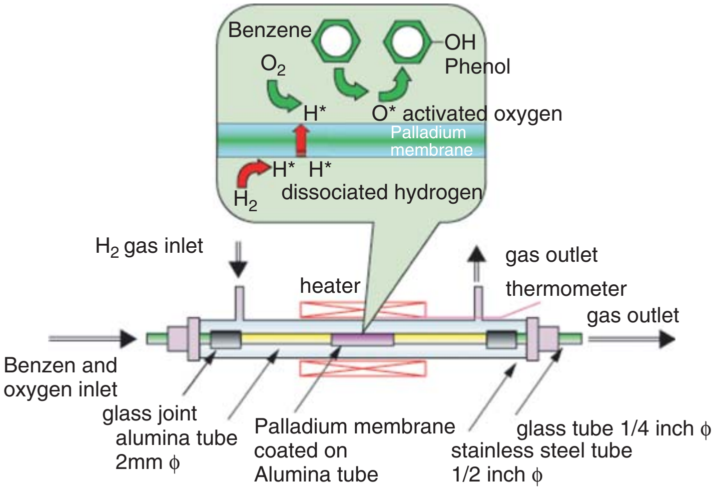

Figure 5.5 *Palladium membrane reactor for the direct synthesis of phenols from benzene in a single-stage reaction. Reproduced from www.aist.go.jp*

an endothermic reaction) the heat generated by the reaction. In this way, an accurate control of the operating temperature is actually attained. Both non-catalytic and catalytic heat-exchanger reactors show interesting promise for (very) fast reactions characterized by high heat of reaction.

5.4.15 Simulated Moving Bed Reactors

The simulated moving-bed reactor combines continuous countercurrent chromatographic separation with chemical reaction (Kundu *et al*., 2009). This hybrid, not energy-intensive process is competitive with traditional processes in which reaction and separation are performed in different units. Higher conversions and better yields can be attained by separating the reaction product(s) in an equilibrium reaction. This technology is applied in those processes where chromatographic separation is a necessary step, that is, when high quality of separation is required and the product has a high value (fine chemicals and pharmaceuticals).

5.4.16 Gas-Solid-Solid Trickle Flow Reactor

In the Gas-Solid-Solid Trickle Flow Reactor fine adsorbent trickles through a fixed bed of catalyst (Kuczynski *et al*., 1987); one or more products are selectively removed from the reaction zone. In case of methanol synthesis, for examples, conversions significantly higher than the equilibrium conversions are achieved under the same operating conditions. The major advantages of this technology are energy savings, increased conversion, and high potential for innovations as given by the utilization of multifunctional catalysis or of structured packing (Muzen and Cassanello, 2007). A current barrier is represented by the fact that, generally, solid recycling is less attractive than liquid or gas recirculation.

5.4.17 Reactive Extraction

Reactive extraction encompasses simultaneous reaction and liquid-liquid separation (Dussan *et al.*, 2010). Reactive extraction may be exploited in multi-reaction systems to attain significant improvements in both yield and selectivity of desired products. This leads to a reduction of both recycle streams and wastes. The combination of reaction and liquid-liquid extraction can be also used for the separation of waste byproducts, which are difficult to remove be conventional methods.

5.4.18 Reactive Absorption

Reactive absorption (Noeres *et al.*, 2003) is actually a mature technique used in the production of nitric or sulfuric acid, for the removal, by amine solutions, of the CO_2 contained in the flue gas, for gas desulfurization, in which H_2S is removed and converted to sulfur, and for the separation of light olefins and paraffins (Ortiz *et al.*, 2010). Reactive absorption is the most applied reactive separation technique.

5.4.19 Reactive Distillation

Reactive Distillation is performed in a conventional distillation column where some species react in the presence of a structured catalyst (Noeres *et al.*, 2002); the obtained products are continuously separated by fractionation, thus favoring the forward reaction; in some cases, even total conversion can be reached. The major benefits of this operation are: lower energy requirements, higher yields, good product purity, and lower capital investment. Reactive distillation may also be exploited as an effective separation method in the case of mixtures containing reactive and non-reactive components with near boiling point (Lai *et al.* 2007). Both homogeneous and heterogeneous catalysis can be applied, even if some problems regarding the catalyst development (performance, kinetics, stability, morphology, coating procedures, etc.) are still to be solved.

5.4.20 Membrane-Assisted Reactive Distillation

In some cases characterized by particular limitations, that is, the presence of an azeotrope, reactive distillation cannot fulfill the desired process performance and another unit operation has to be combined. This could be achieved by coupling a reactive distillation unit to a pervaporation module (Buchaly *et al.*, 2007) so as to further purify the distillate. Two commercial applications have been reported so far, that is the production of methyl borate and the production of fatty acid esters (Kiatkittipong *et al.*, 2011).

5.4.21 Hydrodynamic Cavitation Reactors

The energy associated with a liquid in motion can be successfully utilized to promote cavitation, which is aimed at intensifying reactions and other operations, such as homogenization or emulsification. Figure 5.6 shows a typical hydrodynamic cavitation chamber. Hydrodynamic cavitation can be obtained by allowing the liquid pass through a throttling valve, an orifice plate or any other mechanical constriction (Gogate and Kabadi, 2009). If the operating pressure falls below the cavitation pressure, millions of microcavities are obtained. These bubbles then implode when pressure is

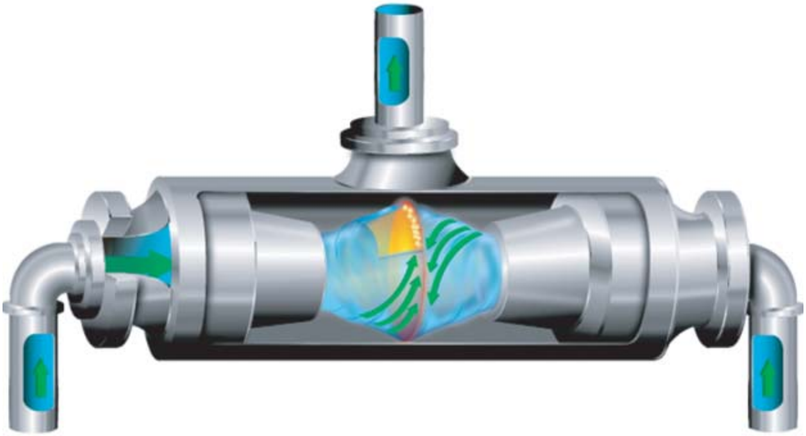

Figure 5.6 Hydrodynamic cavitation chamber. Reproduced from vrtxtech.com

increased. Hydrodynamic cavitation may improve the performance of several industrial transformations, as compared to conventional processes (Gogate and Pandit, 2005). For example, cavitated corn slurry exhibits higher yields in ethanol production as compared to uncavitated corn slurry processing. A significant improvement is achieved also in the mineralization of bio-refractory compounds (Gogate, 2002), which would otherwise need extremely high temperature and pressure conditions to remove the free radicals generated during processing.

5.4.22 Pulsed Compression Reactor

A novel chemical reactor concept derived from PI approach allows a technological breakthrough in syngas production (Roestenberg *et al.*, 2011). This novel concept completely modifies the traditional standpoints since, instead of formulating improved catalysts, which may allow decreasing the operating temperature, no catalyst is used and the reaction is performed at very high temperatures, with peak values in the order of 1500−5000 K (Roestenberg *et al.*, 2010). The reactor consists of a double-ended cylinder and a free piston, which separates the cylinder into two compression-reaction chambers. The piston reciprocates compressing the feed gas, until it reacts, in turn in the lower and in the upper chamber. The reciprocation is maintained by the released reaction energy. This technology, even if it is an early stage of development, could provide an excellent potential for energy savings (reaction energy is directly applied); moreover, CO_2 and NO_x emissions are reduced since feed heating is actually not required. Cost effectiveness is also improved by narrower reaction product distribution (less downstream processing) and more compact reactor area design.

5.4.23 Sonochemical Reactors

In a liquid system the exposure to ultrasound determines, in a time period of a few milliseconds, the formation, growth, and subsequent collapse of microbubbles (Parvizian *et al.*, 2011). The micro-implosions are followed by high energy release, which leads to local generation of extremely high temperatures and pressures, which can be up to 5000 K and 2000 bar, respectively (Sutkar and Gogate, 2009). The use of ultrasound significantly enhances the rate of any chemical reaction, thus increasing the product yield. For chemical syntheses, this technology is in the early stages of its development; however, it may have potentially interesting applications in food processing, biotechnology and environmental protection.

5.4.24 Ultrasound-Enhanced Crystallization

Sonocrystallization is a non-invasive method based on the exploitation of ultrasound to control the point of nucleation and the number of nuclei formed in a crystallization process (Nalajala and Moholkar, 2011). This generally enhances the crystal yields, improves the product properties, namely handling and appearance, reduces the crystal's agglomeration and increases the process reproducibility. An additional advantage is given by the formation of ultra-fine, nano-structured materials; moreover, a significant energy and cost saving can be attained since expensive milling or recrystallization steps are avoided. This technology provides very interesting perspectives in both pharmaceutical and food industry, but reasonably will need about 10–15 years of fundamental research to reach full commercial application.

5.4.25 Electric Field-Enhanced Extraction

Electric fields are commercially employed to increase the process rates and to control the droplet size in pain spraying and in surface coating processes. Other well-known applications regard gas cleaning, emulsion breaking, ink-yet spraying, fuel spraying, crude oil desalting and bulk chemical washing. Electric fields can also enhance liquid-liquid or solid-liquid extraction (Grimi *et al.*, 2007, Gachovska *et al.*, 2010) and improvements of about 200%, as compared to conventional processes, were reported. Typical advantages of this technology are energy savings and equipment size reduction; however, even if well developed for some specific applications, no new innovative products are to be expected in the future.

5.4.26 Induction and Ohmic Heating

Inductive heating is a process where electric currents are induced within a food or any other product due to the presence of oscillating electromagnetic fields generated by electric coils (Sastry and Barach, 2000). Inductive heating is different from microwave heating due to the frequency and the nature of the source. In microwaves in fact, the frequency is specifically assigned and a magnetron (not coils) is used to promote heating. Ohmic heating (also known as Joule heating), electro-conductive heating, or direct electrical resistance heating, involves the direct passage of electric current through a material for the purpose of heating it. Ohmic heating necessarily involves electrodes that are put in contact with the product to create a continuous electrical circuit. The most promising application of Ohmic heating is the continuous sterilization of foods (Goullieux and Pain, 2005) by high-temperature-short-time processing, which yields a significant quality improvement. Figure 5.7 shows a typical ohmic heater exploited in the food industry.

Figure 5.7 Ohmic heater for the food industry. Reproduced from www.kasag.ch

5.4.27 Microwave Drying

In general, microwave frequencies range from 0.3–300 GHz, but, in order to avoid any interference with radar and telecommunication applications, the industrial and domestic microwave appliances operate at a standard allocated frequency, most often at 2.45 GHz. Molecules with a permanent dipole moment (e.g., water) can rotate in a fast changing electric field; in addition, in substances where free ions or ionic species are present, the energy is also transferred by the ionic motion in an oscillating microwave field. As a result of both these mechanisms, the substance is heated directly and almost regularly. The heating extent depends on dielectric properties, namely the dielectric constant and the loss tangent, of the substance to be heated. Some materials absorb the microwave energy very easily; others are transparent or impermeable to it; this may allow a selective heating of materials/products (Holtz *et al.*, 2010). Microwave-enhanced drying is used on industrial scale in food, wood (Bartholme *et al.*, 2009), textile and pharmaceutical industries (Mcloughlin *et al.*, 2000). The speed of the MW drying allows preventing unwanted degradation of some thermo-labile components that it is wanted to preserve in the dried material. Microwave heating allows remarkable energy savings compared to conventional processes. Figure 5.8 shows an industrial-scale microwave oven exploited to achieve wood drying.

5.4.28 Microwave-Enhanced Separation and Microwave Reactors

Microwave heating proved to enhance also some extraction operations, particularly the extraction of pharmaceutical ingredients from plant material. A limited number of papers

Figure 5.8 Microwave oven for wood drying. Reproduced from Jiyuan Electric Co., Ltd.

regarding the enhancement effects of microwaves on membrane separation and distillation have been published as well. The ability of microwave heating to accelerate chemical reactions and to improve the product yield has been extensively reported (Monsef-Mirzai *et al*., 1995). For example, in microwave-assisted oxidative coupling of methane on alumina supported La_2O_3/CeO_2 catalyst conversion occurred at temperatures about 250°C lower than those used by the conventional heating. However, no consolidated data exist on the actual energy/cost savings achievable by microwave reactors.

5.4.29 Photochemical Reactors

Photochemical reactors use the energy of light to initiate or catalyze reactions (Gupta *et al*., 2011). The basic principle is that light quanta are absorbed by chemical species which are excited and become more reactive with regards to other compounds present. The light can originate either from the Sun or from artificial sources, namely medium-pressure mercury or a xenon lamp. In the case of solar photochemical reactors, the energy has to be concentrated so as to attain sufficient efficiency. In non-catalyzed photochemical reactions the light energy is absorbed by a reagent or by a sensitizer, which transfers the electronic energy to the reagent or undergoes a reversible redox reaction with the reagent. Currently, the major applications of photochemical reactors are in production of protective and decorative coatings, inks, packaging, and electronic materials. In other fields, like chemical, pharmaceutical, and food industry the applications are rather rare. The main benefits of this technology regard the use of low temperatures, which means significant energy savings, and very high conversion/yield/selectivity.

5.4.30 Oscillatory Baffled Reactor Technologies

The Oscillatory Baffled Reactor technology generally uses a cylindrical column containing equally spaced orifice baffles and superimposed fluid oscillation (Vilar *et al.*, 2008); this allows plug flow conditions even at low (laminar) flow rates, thus inducing enhanced mass and heat transfers as compared to conventional stirred tank reactors. Vortices are generated when fluid flows through the baffles; the continuous generation and cessation of eddies creates uniform mixing in each baffled cell (Smith and Mackley, 2006). The major advantages of this technology regard a significant energy/utility savings, higher yields and less side product. In addition, capital cost savings are achieved through much more compact designs.

5.4.31 Reverse Flow Reactor Operation

A well-known example of the integration of reaction and heat transfer in a multifunctional single unit is reverse-flow reactors (Simeone *et al.*, 2012) where one or more process variables are intentionally and continuously perturbed (see Fig. 5.9); this dynamic operation results in process improvements, which cannot be achieved by steady state operation. In the case of exothermic processes the periodic flow reversal, typical of such systems, allows for a very good utilization of the heat of reaction, which is maintained within the catalyst bed and, after the reversion of the flow, is used to pre-heat the stream of cold reactants entering the reactor. So far, the reverse-flow reactors have been used in the SO_2 oxidation (Gosiewski, 1993), in the total oxidation of hydrocarbons contained in the off-gases and in the NO_x reduction (Botar-Jid *et al.*, 2007). The major benefits of this technology are represented by energy savings, increased conversion selectivity, and enhanced productivity.

5.4.32 Pulse Combustion Drying

The term pulse combustion originates from the intermittent combustion of the solid, liquid, or gaseous fuel in contrast to the continuous combustion that occurs in conventional burners (Zbiciński *et al.*, 2001). Such periodic combustion generates pressure,

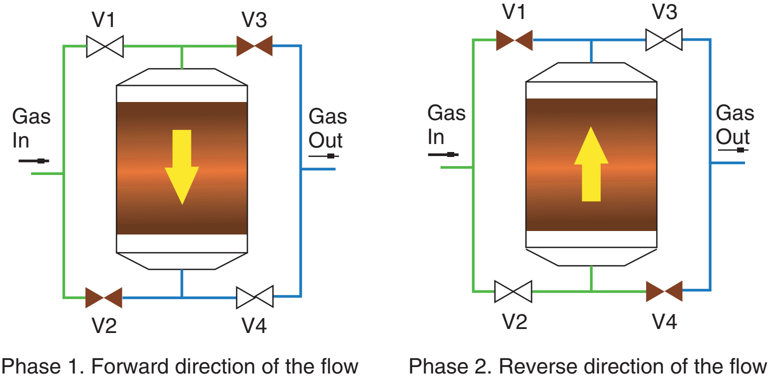

Figure 5.9 Reverse flow reactor operation. Reproduced from www.matrostech.com

velocity, and temperature waves which propagate from the combustion chamber to the drying chamber. Due to such wave propagation, the rates of heat and mass transfer and, consequently the drying rate, are significantly improved as compared to conventional processes. The pulse combustion dryer consists of a pulse combustor combined to a spray dryer or a rotary kiln or a fluid-bed dryer (Zbiciński, 2002). Pulse combustion drying represents an energy-efficient and environmentally-friendly technology; as compared to traditional spray dryers, it indeed provides lower energy consumption, lower capital cost, and lower CO_2 emission. In spite of these advantages, the application of pulse combustion is not widespread.

5.4.33 Supercritical Separation

Supercritical fluids have some properties, for example, density, that are quite similar to those of a liquid, and some other properties, such as low viscosity, low surface tension, and high diffusivities for solutes, which makes them similar to a gas (Gere *et al*., 1997). This is due to the fact that above the supercritical point there is no difference between the phases. Supercritical fluids, due to their unique properties, may significantly improve the performance of some conventional separation processes, like for example extraction. In fact, some compounds which are almost insoluble in a fluid at ambient conditions can become soluble in the fluid at supercritical conditions (see Fig. 5.10). Currently CO_2 is mostly used but other compounds, namely hexane, pentane, and ammonia, can be

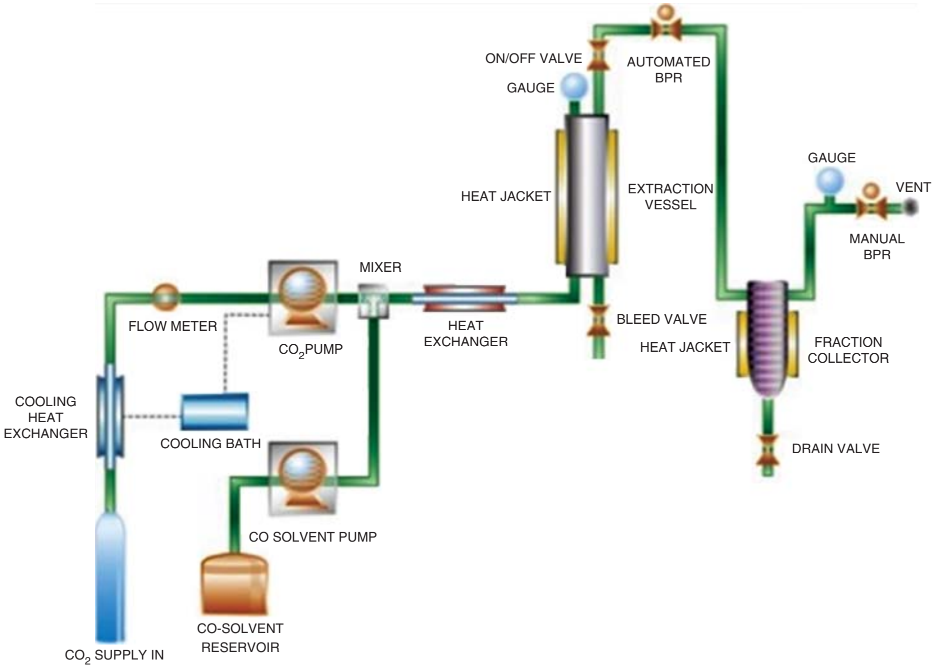

Figure 5.10 *Supercritical fluid extraction system. Reproduced from www.waters.com*

exploited as well. Supercritical separations using CO_2 are well established in extraction of natural materials (Reverchon, 1997). By using CO_2 in supercritical conditions, that is, when the substance is like a liquid, high value compounds can be extracted from mixtures; after pressure reduction, the supercritical fluid becomes a gas and the compounds can be recovered in a pure/not dissolved form. The major benefit is therefore represented by the avoidance of a traditional solvent and its associated waste problems, that is, emissions to the atmosphere or waste treatment.

5.5 Conclusions

Process intensification is a valuable tool for the development of more sophisticated and more efficient processes aimed at sustainable production in industry. Process intensification methodologies have already offered substantial benefits in material and energy efficiency, and the contribution of PI concepts was fundamental in designing novel types of equipment and of processes. Further improvements can be attained if operation and control of a complete process are considered simultaneously and systematically together with different PI design options. In order to find true optimal configuration it is also necessary to exploit a rigorous methodology, which allows determining intensified options by stepwise reduction of the search space through constraints, performance evaluation and objective function. In this context, a set of PI metrics accounting for economic, environmental, safety and process performance has to be developed to compare, on the basis of precise modeling techniques, different possible options, which allow intensifying a process through a standard set of performance measures.

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1
Chemistry for Development

Stephen A. Matlin and Berhanu M. Abegaz

1.1
Chemistry, Innovation and Impact

The foundations of modern chemistry were laid in the 18th and 19th centuries and further extended in the 20th century. They encompassed the development of a theoretical framework for understanding and explaining the physical and chemical properties of atoms and molecules, together with the invention of increasingly sophisticated techniques for interacting with these entities in order to study and influence their structures and behaviors. These developments have given humanity a degree of mastery over its physical environment that surpasses the sum of achievements over the entire previous period of human history.

Chemistry's contributions to human advancement need to be seen in terms of its own core role as a physical science, but also as a "platform science" in the context of its relationships within the group of "natural sciences" that includes physics and biology. Chemistry provides the basis for understanding the atomic and molecular aspects of these disciplines and, through its interfaces with a range of pure and applied sciences, underpins the dramatic advances seen in recent decades in such diverse fields as medicine, genetics, biotechnology, materials and energy. Hence, this discussion of the role of chemistry in the process of development is framed in the broader context of the roles of science, technology and innovation more generally.

Innovation, which may operate in both technological and social fields [1], encompasses not only the birth of an idea or a discovery, but its application in practice – taking the outputs of research and invention and using them to put new goods, services or processes into use. While innovation is sometimes represented as a straightforward linear system (Figure 1.1), in reality this is an over-simplified model and innovation needs to be treated as a complex, highly nonlinear ecosystem, full of interdependences and feedback loops.

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Edited by Javier Garcia-Martinez, Elena Serrano-Torregrosa

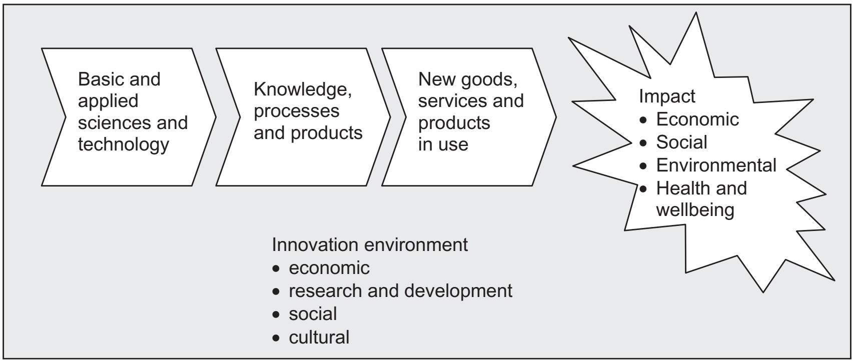


Figure 1.1 The chain of scientific innovation – from ideas to impact.

Chemistry may be involved not only in the initial stages of research (e.g., in areas such as agrochemicals and pharmaceuticals: chemical synthesis of new molecules for testing), but also in intermediate stages (e.g., product development, quality control) and in the evaluation of impact (e.g., health status assessment, environmental monitoring), thus contributing in key ways at every stage of the technological innovation chain.

Throughout the modern period of its development, chemistry has contributed enormously both to broad improvements in human wellbeing (including enhancements of health and quality of life) and to wealth creation for individuals and nations. Some landmark examples are summarized in Table 1.1. Early developments in electrochemistry and synergies with physics and engineering led to methods for producing electrical energy, which has impacted on virtually every aspect of human activity. Electrochemistry also provided the basis for the industrial transformation of many materials and, in particular, for the production of metals such as aluminum and important feedstocks such as caustic soda and chlorine. Industrial organic chemistry built on mid-19th century processes for manufacturing dyestuffs, but by the 20th century had expanded to include the synthesis of pharmaceuticals. In parallel with advances in public health (measures for reducing the spread of infectious diseases through improved water, sanitation and vaccination; and for improving health through ensuring optimal nutrition – in all of which areas chemistry has played a major role), pharmaceutical chemistry has contributed enormously to improving life expectancy and the quality of life through the treatment of infectious diseases and metabolic disorders and the control of pain. Chemistry has contributed to many of the advances in agriculture (e.g., fertilizers, plant growth regulators, pesticides) which have been characterized as a “green revolution” and which have helped to feed the world’s population while it grew from about 1 billion to 6 billion during the 20th century. Moreover, chemistry has given the world a wide array of new materials, including polymers, plastics, semiconductors and superconductors, with applications from fabrics and structural materials to information and communications technologies and medical imaging.

Table 1.1 Landmark examples of chemistry breakthroughs contributing to health and wealth.

Date	Scientist	Breakthrough	Impact	Refs
		Industrial chemistry, electrochemistry, power and light		
1800	Alessandro Volta	Discovered that a continuous flow of electricity was generated when using certain fluids as conductors to promote a chemical reaction between the metals or electrodes.	Mass production of portable power sources enabled a vast range of applications– from automobiles to radios. The nickel–metal hydride battery, commercialized in 1990, provided a high energy density and absence of toxic metals. It has found numerous applications include mobile phones and laptop computers	[2]
1802	William Cruickshank	Designed the first electric battery capable of mass production.		
1839	William Grove	Invented the H_2/O_2 fuel cell.		
1859	Gaston Platé	Invented the first rechargeable battery, based on lead-acid chemistry.		
1806	Humphry Davy	Connected a very powerful electric battery to charcoal electrodes and produced “the most brilliant ascending arch of light ever seen”.	Invention of the electric light bulb paved the way for replacement of polluting combustion processes for lighting and enabled mass lighting in homes, workplaces and public spaces.	[2]
1879	Thomas Edison	Discovered that a carbon filament in an oxygen-free bulb glowed but did not burn up.		
1820	André-Marie Ampère	Observed that wires carrying an electric current attracted or repelled one another.	Invention of the electric generator transformed life in industrialized countries, impacting on transport, work and leisure.	[2]
1831	Michael Faraday	Demonstrated that a copper disc was able to provide a constant flow of electricity when revolved in a strong magnetic field.		
1800	William Cruickshank	First description of electrolysis of brine	Electrolysis became an extremely important method of transforming materials and especially for the production of inorganic chemicals and compounds, either for use in their own right (e.g., see entry on aluminum below) as a source of feedstocks for the manufacture of other compounds, including organics. For example, the chlorine by-product from the electrolysis of brine was the starting point for the manufacture of organic compounds including solvents, pesticides and plastics	[2–4]
1833	Michael Faraday	Formulation of the laws that govern the electrolysis of aqueous solutions		
1861	Ernest Solvay (1838–1922)	Patented Solvay Process for manufacture of industrial soda using carbon dioxide, brine and ammonia. After the first commercial plant for the electrolysis of brine was built in 1891, caustic soda was increasingly produced directly by this method.		
1897	Herbert Dow	Dow persuaded a group of Cleveland investors to back him in building a chloralkali business in Midland, to be known as The Dow Chemical Co.		

Table 1.1 *Continued*

Date	Scientist	Breakthrough	Impact	Refs
1825	Hans Christian Oersted	Metallic aluminum first made by heating potassium amalgam with aluminum chloride.	Due to its low density, high thermal and electrical conductivity, non-magnetic character, high ductility and the capacity of the metal and its alloys to be cast, rolled, extruded, forged, drawn, and machined, aluminum became one of the most important and ubiquitous metals in the 20th century.	[5] [6]
1886	Charles Hall Paul Heroult	Electrolytic processes for the production of aluminum.		
1840s	August Hoffman	Discovery of aniline and process for its synthesis from benzene	Aniline dyes became the basis for the development of the dyestuffs industry in the 19th century, leading to major growth in chemical industries in the UK, France and Germany.	[7]
1856	William Perkin	Invention of mauve dye (aniline purple).		
		Medicinal chemistry and medicine		
1853	Charles Gerhardt	First synthesis of acetylsalicylic acid	Studies of microorganisms and the physiological effects of chemicals and work on the structural modification of natural products and synthetic chemicals in the 19th century laid the foundations for the pharmaceutical industry in the 20th century. Major classes of therapeutic agents soon emerged, including analgesics, anaesthetics, anti-infectives and anti-tumor agents.	[8–18]
1897	Felix Hoffmann	Investigated acetylsalicylic acid as a less-irritating replacement for salicylate medicines, e.g., for treating rheumatism.		
1860–1864	Louis Pasteur	Demonstrated that fermentation is caused by specific microorganisms and formulated the germ theory of disease – providing the basis for biotechnology and anti-microbial chemotherapy.	Growing understanding of the chemistry of metabolic processes and of the structures and functions of proteins and nucleic acids all contributed to the evolution of pharmacology and molecular biology as distinct sciences and to drug targeting and rational drug design.	
1909	Paul Ehrlich	Synthesis of anti-syphilis organo-arsenical drug, Salvarsan.		
1928 1940	Alexander Fleming Howard Florey Ernst Chain	Discovery of penicillin, the first of a family of β-lactam antibiotics, and development of large-scale process for its production		
1932	Gerhard Domagk	Began testing Prontosil, leading to development of the sulfonamide antibiotics	Understanding of the metabolic roles of vitamins and hormones paved the way for a range of drug therapies for metabolic disorders and for development of hormonal contraceptives.	

Table 1.1 *Continued*

Date	Scientist	Breakthrough	Impact	Refs
1865	Heinrich Lissauer	Used potassium arsenite to treat chronic myelogenous leukemia – the first instance of effective chemotherapy for malignant disease. The modern era of cancer chemotherapy began with the study of the cytotoxic effects of nitrogen mustards on lymphoid tissues by Alfred Gilman, Louis Goodman and coworkers in the 1940s.	The pharmaceutical industry now employs well over half a million people and generates global sales in excess of US$ 700 billion per year. In the UK alone, the industry provided employment for 67 000 workers in 2007.	
1912	Casimir Funk	Published the “vitamine theory”, based on observations of the effects of depriving animals of small amounts of essential dietary chemicals. Paved the way for the modern understanding of vitamins and their roles as key biochemical catalysts.		
1901	Jokichi Takamine	First isolation of epinephrine.		
1915	Edward Kendall	First isolation in crystalline form of thyroxine from thyroid gland.		
1921–22	Frederick Banting John McLeod Charles Best	First isolation of insulin and demonstration of its capacity to treat diabetes.		
1951	Carl Djerassi	Synthesized norethindrone, the first effective oral contraceptive.		
1949	Linus Pauling, Harvey Itano, S. J. Singer, Ibert Wells	Publication of “Sickle Cell Anemia, a Molecular Disease” – the first proof of a human disease caused by an abnormal protein and the dawn of molecular genetics.		
1953	James Watson Francis Crick	Discovery of the double helix structure of DNA – the foundation of molecular biology.		
1955	Frederick Sanger	First determination of the complete amino acid sequence of a protein – insulin.		
1958	Max Perutz John Kendrew	First three-dimensional structures of proteins solved by X-ray crystallography – hemoglobin and myoglobin.		

Table 1.1 *Continued*

Date	Scientist	Breakthrough	Impact	Refs
		Dentistry		
1826	Auguste Taveau	First to use amalgam as a dental restorative material	The development of safe and effective materials for dental restoration and anesthesia transformed dentistry, which had hitherto been a crude and extremely painful procedure.	[19]
1844–1846	Horace Wells William Morton	First uses of nitrous oxide and ether as general anesthetics for dental extractions		
1901	Frederick McKay	Began investigating the cause of widespread brown staining of teeth in Colorado Springs, which he discovered was associated with a dramatic absence of dental caries. Work by chemists in the 1930s eventually traced the cause to fluoride in drinking water.	Water fluoridation and the development of fluoride-containing toothpastes have further contributed to a dramatic improvement in oral health in many countries.	
1905	Alfred Einhorn	First synthesis of procaine (novocaine), a synthetic analog of cocaine without its addictive properties and the first safe local anesthetic for dentistry.		
		Agrochemistry		
1909	Fritz Haber	Invented the Haber process for nitrogen fixation, later scaled up by Carl Bosch. Fixation of nitrogen as ammonia, which can then be oxidized to make nitrates and nitrites, made possible the industrial production of many classes of compounds including nitrate fertilizers and explosives.	The Haber process now produces 100 million tons of nitrogen fertilizer per year, consuming 3–5% of world natural gas production (ca. 1–2% of the world's annual energy supply) and generating fertilizer which is responsible for sustaining one-third of the Earth's population.	[20] [21] [22] [23] [24] [25]
1874	Othmar Zeidler	First synthesis of DDT.	The development of plant growth promoters, crop protection agents and agents promoting animal health contributed to an agrochemicals industry with global annual sales of over of US$ 100 billion and, together with advances in plant breeding and agronomy methods, produced the green revolution of the 1960s–1980s which has helped feed the burgeoning population of the planet.	
1939	Paul Müller	Insecticidal properties discovered. DDT became the first commercial organochlorine insecticide. Prior to its banning on environmental grounds, DDT was a major weapon in the fight to eliminate malaria.		
1951	Geigy Chemical Co.	Introduction of carbamate insecticides		
1960s	Michael Elliott	Development of synthetic pyrethroid insecticides.		

Table 1.1 *Continued*

Date	Scientist	Breakthrough	Impact	Refs
		Analytical chemistry		
1901	Michael Tswett	First use of an adsorption column for the separation of plant pigments marked the birth of chromatography – later to develop into a family of 2- and 3-dimensional techniques involving combinations of gas, liquid and solid phases, for analytical and preparative scale separation of compounds.	The pioneering studies by a range of scientists, including botanists, physicists and physical chemists, led to the development of extremely powerful sets of techniques for separating chemical species, identifying them and measuring their concentrations. The evolving and often intertwined fields of analytical and separation sciences have been of fundamental importance, not only to the advance of chemistry itself but also to a wide range of areas including clinical and environmental sciences.	[26] [27] [28] [29] [30] [31]
1800	William Herschel	Discovered infrared radiation.		
1854	August Beer	Extending earlier work by by Pierre Bouguer and Johann Lambert, published what became known as the Beer-Lambert Law, defining the relationship between the extent of absorption of light and the properties of the material through which it is traveling.		
1859	Robert Bunsen Gustav Kirchoff	Developed the first spectroscope.		
1895	Wilhelm Röntgen	First systematic studies of X-rays, which later became the basis of X-ray medical diagnosis and X-ray crystallography.		
1913	Joseph Thomson	Invented mass spectrometry.		
1938	Isidor Rabi	First described and measured nuclear magnetic resonance in molecular beams. NMR became the basis of techniques for molecular structure elucidation and also medical imaging.		

Table 1.1 *Continued*

Date	Scientist	Breakthrough	Impact	Refs
		Polymers and plastics		
1839	Charles Goodyear	Discovered the process of vulcanization of natural rubber by heating with sulfur	Materials based on synthetic plastics and polymers became ubiquitous in the 20th century, finding applications in clothing, products from containers and appliance casings to non-stick pans, thermal and electrical insulators, components of transport machinery, medical and surgical devices, in space exploration and in much else.	[32] [33] [34] [35] [36]
1855	Alexander Parkes	Created the first plastic by treating cellulose treated with nitric acid.		
1909	Leo Hendrik Baekeland	Bakelite, the first synthetic polymer plastic, made from phenol and formaldehyde.		
1934	Wallace Carothers	First synthesis of a synthetic fiber, nylon, by co-polymerization of hexamethylene diamine and adipic acid		
		Solid state chemistry		
1833	Michael Faraday	Described first semiconductor effect, noting that electrical conductivity in silver sulfide increased with increasing temperature	Semiconductors based on silicon became the basis of solid state electronic devices including computers and provided the foundation for the modern digital age.	[37]

The value added by these products of chemistry and related sciences has contributed to the rapid growth in world GDP [38], especially in the industrially advanced countries during the second half of the 20th century (Figure 1.2). Knowledge-intensive and technology-intensive industries are estimated [39] to have accounted for 30% of global economic output, or some US$15.7 trillion, in 2007.

1.2
Poverty and Disparities in Life Expectancy

The benefits from advances in chemistry and other sciences have not been evenly distributed globally. The least industrially/technologically advanced countries have remained the poorest and people in the low- and middle-income countries (LMICs) have often fared worse than those in high-income countries (HICs), as illustrated by the dramatic relationship between poverty and life expectancy: the poor die young. Life expectancies around the world have increased very markedly over the course of the last century, but as they have done so the disparities between populations have grown larger [40]. However, the relationship between life expectancy

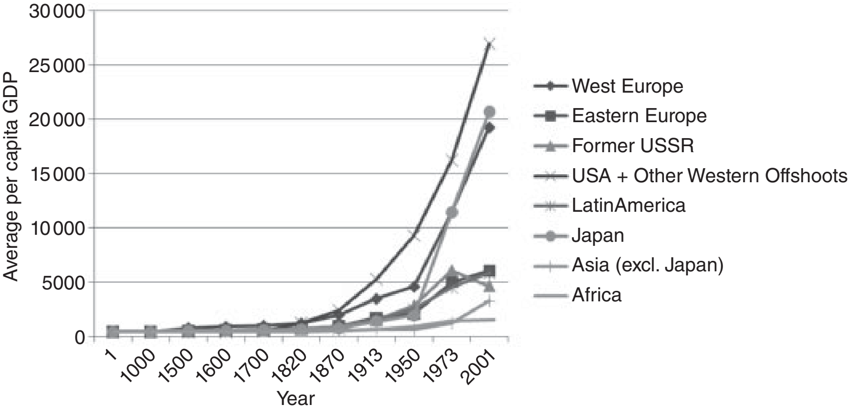


Figure 1.2 Per capita GDP: Regional and world averages, 1–2001 AD (millions 1990 international Geary-Khamis dollars). Data from [38], Table 8c.

and the average per capita income of the country is not a straightforward one and income is not the only factor involved. The economist Easterlin [41] concluded that much of the decline in mortality in the 20th century had its origin in technical progress – and in this context, "technical progress" refers to a combination of technological advances and their diffusion and uptake in different countries and the capacities of the countries themselves to conduct and apply research. Much of the variation in life expectancies seen between countries is explained by differences in the rate of this technical progress – for example, it explains two thirds of the variation in the decline in infant mortality over a 25 year period, whereas change in income explains only 9% [42, 43].

1.3
The Millennium Development Goals

In response to the unacceptable levels of poverty (Box 1.1) and growing disparities in health and wellbeing between people in different countries, the world's

Box 1.1 Poverty

What is poverty?

Poverty is hunger. Poverty is lack of shelter. Poverty is being sick and not being able to see a doctor. Poverty is not having access to school and not knowing how to read. Poverty is not having a job, is fear for the future, living one day at a time. Poverty is losing a child to illness brought about by unclean water. Poverty is powerlessness, lack of representation and freedom.

The World Bank [46]

governments met at the Millennium Summit [44] in New York on 6–8 September 2000, issuing the Millennium Declaration which led to agreement on a series of Millennium Development Goals (MDGs) [45] that were set for 2015 (Table 1.2). The targets were acknowledged to be extremely ambitious – but it was recognized that, for the first time in history, mankind had the capacity to substantially reduce or eliminate many sources of human suffering and to offer every person on the planet a basic level of existence that would be free from hunger, disease and discrimination in access to opportunities for development.

As stated in the report of the Task Force on Science Technology and Innovation of the Millennium Project [47]:

> "Since their adoption at the United Nations Millennium Summit in 2000, the Millennium Development Goals have become the international standard of reference for measuring and tracking improvements in the human condition in developing countries. The Goals are backed by a political mandate agreed by the leaders of all UN member states. They offer a comprehensive and multidimensional development framework and set clear quantifiable targets to be achieved by 2015."

The latest assessment shows that uneven progress has been made towards meeting the targets. Unmet commitments, inadequate resources, lack of focus and accountability and insufficient dedication to sustainable development have created shortfalls in many areas and without a major push forward many of the MDG targets are likely to be missed in most regions [48].

To achieve the goals will require a collective global effort harnessing political will, available resources and innovation in all areas, including the application of science and technology.

1.3.1
Goal 1: Reducing Poverty and Hunger

Economic growth, especially in the world's most populace country, China, resulted in hundreds of millions of people being lifted out of poverty during the last quarter of the 20th century [46]. Nevertheless, at the end of the century, out of a global population of 6 billion there were more than one billion people living on less than \$1 a day, more than three billion living on less than \$2 a day and nearly a billion suffering from hunger or severe malnutrition.

While many economically advanced countries produce an excess of food, some of which goes to waste, halving the proportions of those suffering poverty or hunger by 2015 is not merely a matter of redistributing available food. To overcome the net food shortage, allow for the expanding world population (already approaching 7 billion by 2010), ensure food security and independence from aid handouts, and respond to the agricultural impacts of climate change, it is necessary to expand agriculture throughout the world. Better applications of existing technologies and development of innovative new ones are essential

Table 1.2 Millennium development goals.

Goals	Targets
Goal 1 Eradicate extreme poverty and hunger	Halve, between 1990 and 2015, the proportion of people whose income is less than $1 a day Halve, between 1990 and 2015, the proportion of people who suffer from hunger
Goal 2 Achieve universal primary education	Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling
Goal 3 Promote gender equality and empower women	Eliminate gender disparity in primary and secondary education preferably by 2005 and in all levels of education no later than 2015
Goal 4 Reduce child mortality	Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate
Goal 5 Improve maternal health	Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio
Goal 6 Combat HIV/AIDS, malaria and other diseases	Have halted by 2015 and begun to reverse the spread of HIV/AIDS Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases
Goal 7 Ensure environmental sustainability	Integrate the principles of sustainable development into country policies and programmes and reverse the loss of environmental resources Halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation Have achieved, by 2020, a significant improvement in the lives of at least 100 million slum dwellers
Goal 8 Develop a global partnership for development	Develop further an open, rule-based, predictable, non-discriminatory trading and financial system (includes a commitment to good governance, development, and poverty reduction – both nationally and internationally) Address the special needs of the least developed countries (includes tariff-and quota-free access for exports, enhanced program of debt relief for HIPC and cancellation of official bilateral debt, and more generous ODA for countries committed to poverty reduction) Address the special needs of landlocked countries and small island developing states (through the Program of Action for the Sustainable Development of Small Island Developing States and 22nd General Assembly provisions) Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term In cooperation with developing countries, develop and implement strategies for decent and productive work for youth In cooperation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries In cooperation with the private sector, make available the benefits of new technologies, especially information and communications

[49] – amounting to a second "green revolution" in which chemistry must play multiple important roles. Critical areas include improving plant varieties and methods for the efficient production, processing and preservation of foods that are healthy and nutritious.

The poverty goal is often referred to as an overarching goal, as it is intimately associated with the problems that are tackled in the other goals, including lack of gender equality, poor education and illiteracy, unacceptably high rates of maternal, neonatal and child mortality and of deaths from infectious diseases, lack of access to improved water and sanitation, and poor environment. However, it would be wrong to focus excessively on achieving this goal in the hope that the others will be met as a consequence. Other areas, such as education and health, have also been stressed as fundamental enablers of progress and the barriers to reaching each goal are varied and complex in nature, requiring individual attention. The reality is that effort is necessary across the whole range of issues highlighted in the MDGs. It must also be stressed that the MDGs are by no means comprehensive or complete, if a permanent shift in the trajectory of human development is to be achieved – for example, the MDGs make no direct reference to overcoming the challenges of unmet needs for reproductive health or the burgeoning rates of non-communicable diseases in LMICs.

1.3.2
Goal 2: Achieving Universal Primary Education

Education is a fundamental enabler of many other aspects of human development. Access to literacy, numeracy and knowledge transforms the lives of individuals, leading to better health and enhancing economic and social advancement, as well as contributing to national economic development. Yet, in the year 2000, there were more than 110 million children of primary school age out of school [50], a very low standard of education available for many children officially attending schools in some countries, and many hundreds of millions of adults who were illiterate. Moreover, education has exhibited a very high degree of gender discrimination, with a majority of those lacking access being girls and women. The high importance of education warrants the goal of ensuring universal primary schooling as a first step towards enabling access to secondary and further education.

1.3.3
Goal 3: Promoting Gender Equality and Empowering Women

Discrimination in access to education and health services and economic, social and political opportunities is experienced by girls and women in every part of the world. The fundamental right of females to equality of status, opportunity and treatment in all areas of human endeavor was established by a series of UN conventions and intergovernmental declarations during the 20th century [51–54], but at the close of the millennium the reality of women's and girls' experiences fell very far short of these standards in many parts of the world, and especially in many low- and middle-income countries. The MDGs set specific targets for moving towards gender equity, to help drive the process forward. Among the areas highlighted for urgent action was access to education – and it is notable that, even for girls enrolled in education, they often experience barriers in access to science and technology education in many countries [55].

1.3.4
Goals 4 and 5: Reducing Maternal and Under-Five Child Mortality

The chances of a woman dying during pregnancy or childbirth or in the immediate post-partum period, or of a child dying in the first few years of life, can be a hundred-fold greater in some of the world's poorest countries than in some of the richest. The causes, which link to poverty, poor nutrition, lack of education and inadequate availability of and access to effective health services including emergency obstetric care, may be varied. However, they are well understood and it is unacceptable in the 21st century that women should continue to die in large numbers simply because they become pregnant or that infants should die because they are not provided with the means of survival. The latest assessments [56] show some progress, but maternal and child mortality levels in many LMICs remain unacceptably high (Figure 1.3) and many countries are still off track to meet the MDG targets.

1.3.5
Goal 6: Combating HIV/AIDS, Malaria and Other Diseases

The development of antibiotics and vaccines has contributed to a massive reduction in mortality and morbidity due to infectious diseases in high-income countries during the last hundred years. However, many LMICs continued to experience major problems with communicable diseases – especially those caused by tropical parasitic infections such as malaria, leishmaniasis, trypanosomiasis, schistosomiasis and Guinea Worm. The advent of the HIV/AIDS epidemic, which began spreading rapidly in countries in Africa and elsewhere in the 1980s and 1990s, transformed the situation into one of crisis, compounded by the concomitant resurgence of tuberculosis in increasingly drug-resistant forms. Meeting the targets for halting and rolling back the spread of these diseases requires not just better access to existing technologies but also, in many cases, innovations in the form of new diagnostics, drugs, vaccines and delivery systems – all areas where chemical sciences must make a core contribution.

1.3.6
Goal 7: Ensuring Environmental Sustainability

The broad concept of "sustainable development" – recognizing the finite nature of the world's physical and biological resources and the importance of protecting and preserving them while engaging in human activity on the planet – emerged during

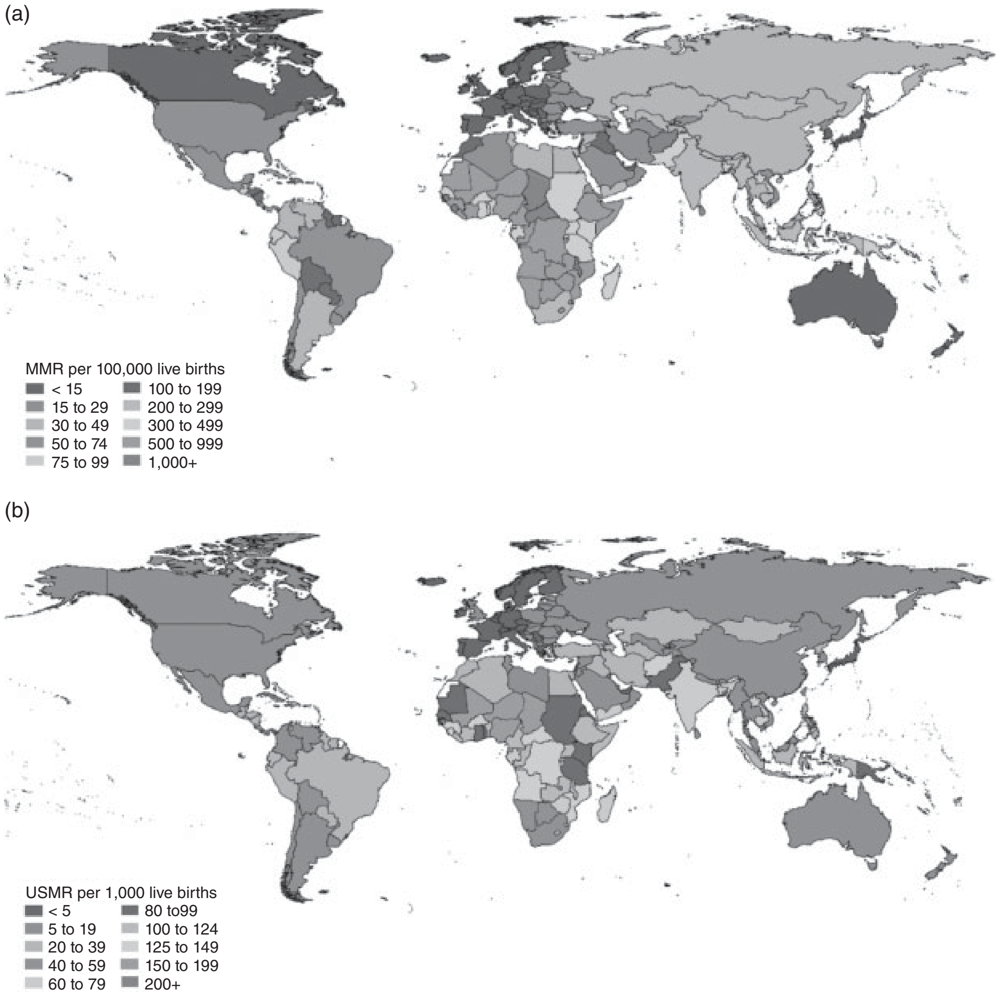


Figure 1.3 (a) Maternal mortality ratio (MMR) by country (per 100 000 live births), 2008 and (b) under-5 mortality rate (U5MR) by country (per 1000 live births), 2008 (from [56]). (Please find a color version of this figure in the color plates.)

the second half of the last century and was the focus of attention in world summits in Rio de Janeiro in 1992 [57] and in Johannesburg in 2002 [58]. The MDG targets represent an attempt to make some headway with these extremely challenging problems.

While there was still dispute at the end of the 20th century about the degree of climate change that the world would experience, there is now conclusive evidence that global warming is a real phenomenon and that climate change is already having, and will continue to have, increasingly severe impacts on many aspects of the human condition, including health, agriculture, the availability of fresh water, human habitation and, especially for some low-lying countries, even their very existence [59].

A further important aspect of the changing human environment has been a major shift during the last century from rural to urban dwelling. In 2007, for the first time, the proportion of human beings living in urban dwellings reached 50% and the transition continues [60]. Since most of the increase in the world population expected to occur during the next half century (from 6 billion in 2000 to 9 billion in 2050) will take place in LMICs, and since cities in many of these countries already have a high proportion of their inhabitants living in slum conditions without adequate water or sanitation, the challenges for city planners and technologists are enormous.

1.3.7
Goal 8: Developing a Global Partnership for Development

Globalization (the increasingly rapid and less restricted movement of people, goods, services and information around the world) brings with it a growing global interdependence of people and economies. This has resulted in a pressing need for global systems governing a wide range of human activities that impact on health, trade, the environment and much else. The eighth MDG calls for effective global partnerships among all the relevant actors to address a range of concerns that were seen to be important at the opening of the new millennium, including the rules governing access to health technologies and to information and communications technologies.

One aspect of health technology that has attracted much attention has been the issue of how the rules governing intellectual property rights should be applied justly and humanely in the field of medicine, considering the high costs of anti-retroviral drugs for the treatment of people living with HIV/AIDS and other life-threatening diseases [61]. The eighth MDG looks to governments and pharmaceutical companies to cooperate in providing access to affordable essential drugs in LMICs.

1.4
Science, Technology and Development

Advances in science and technology (S&T) enabled countries in Europe and North America to industrialize rapidly in the 19th and 20th centuries. For example, industrialization in Belgium drew on the Solvay process for manufacture of soda, which helped to establish Belgium as one of the world's leading countries in the chemical industry sector (Box 1.2).

While this process in Europe and North America was under way, from as early as the end of the 19th century a number of less developed countries were beginning to recognize the importance of S&T, either for economic growth or to address serious health challenges such as epidemics. Some notable examples include:

Box 1.2 Chemistry and the industrialization of Belgium

The industrial revolution began in Belgium with the development of British-style machine shops at Liège (*ca.* 1807), and Belgium became the first country in continental Europe to be transformed economically. Like its English counterpart, the Belgian industrial revolution initially centered on iron, coal and textiles. During the 19th century the chemical industry added momentum to Belgium's industrial and economic development.

Ernest Solvay (1838–1922) developed a process for manufacturing industrial soda (sodium carbonate), in which carbon dioxide (from limestone) is mixed with sodium chloride solution and ammonia. The Solvay process, which was cheaper and more efficient than the old Leblanc process, was patented in 1861 and Solvay opened his first factory at Couillet in Belgium in 1863. Industrial soda is used in manufacturing glass, steel and detergents and demand was huge. By 1900, the Solvay process was used to manufacture 95% of the world's industrial soda, and Solvay had an extensive business empire, with factories in Europe and the USA. Today, around 70 plants using the Solvay process are in operation around the world.

As demand increased, in 1898 Solvay started producing caustic soda directly by the electrolysis of brine, a process which also yields chlorine and hydrogen and gradually replaced the older method. The chlorine was used to produce hydrochloric acid, sodium hypochlorite and, later, organic derivatives including vinyl chloride (the monomeric precursor of PVC plastics); while the hydrogen was oxidized to hydrogen peroxide. Solvay is now the world's leading producer of peroxygen-based products, with a global network of peroxygen production plants.

In 2007, on a per capita basis Belgium was the number one producer of chemicals in the world and the share of the chemical industry in Belgium's economy was even bigger than that in Germany [62, 63].

- A number of research institutions established branches or offshoots in less industrialized countries. In particular, France's Institut Pasteur, created in 1887 for the prevention and treatment of infectious diseases through research, teaching and public health initiatives, established an international network which currently counts 30 members spread over the five continents [64]. Early members of the network included Pasteur institutes in Vietnam (1891), Tunisia (1893), Algeria (1894), Madagascar (1898), Morocco (1911), Iran (1920), Senegal (1923) and French Guiana (1940).
- Conceived in 1896 by Jamsetji Nusserwanji Tata and finally born in 1909, the Indian Institute of Science was an early example of a research institute established in the British colonial period [65]. The South African Chemical Institute [66] was founded in 1912.
- Brazil's Federal Seropathy Institute, established in 1900 to produce serums and vaccines against the plague, in 1908 became the Oswaldo Cruz Institute and later the Oswaldo Cruz Foundation [67]. It has made huge contributions to combating disease, including through the production of medicines by its Farmanguinhos branch [68].

- Rubber Research Institutes were established to support the expanding demand for rubber products. For example, the origin of research on rubber in Sri Lanka dates from 1909, when a group of planters in the Kalutara District met and agreed to engage a chemist to study the coagulation of rubber [69]. Similarly, Rubber Research Institutes emerged in other rubber-growing countries, including Nigeria [70] (1900), Malaya [71] (1925) and India [72] (1946).

Since the mid-20th century, the importance of science and technology for development has increasingly been recognized by international agencies [73–75], development assistance partners [76] and the governments of LMICs [77–79].

Within the UN family, UNESCO is the UN specialized agency mandated to build institutional and human capacity in the basic and engineering sciences, which are seen as a prerequisite for social and economic development. UNESCO's activities focus principally on third-level, but also second-level, education and on research in mathematics, physics, chemistry, biology, biotechnology and basic medical sciences [80]. The UNESCO Science Prize is awarded biennially to "a person or group of persons for an outstanding contribution they have made to the technological development of a developing member state or region through the application of scientific and technological research (particularly in the fields of education, engineering and industrial development)." The first prize was awarded to Robert Simpson Silver in 1968 for his discovery of a process for the demineralization of sea water; several subsequent prizes have also been chemistry-related [81]. A partnership between UNESCO and L'Oréal, *Awards For Women in Science*, forms a core element of UNESCO national and international activities to foster gender equality and equity in science [80].

The work of UNESCO is reinforced by the recognition by the UN Development Programme (UNDP) of the importance of technology for the progress of the least developed countries [82].

A number of nongovernmental organizations (NGOs) have been established to promote the roles in development of S&T in general. Some notable examples include:

- **Academy of Sciences for the Developing World (**TWAS**: originally known as the** Third World Academy of Sciences**):** TWAS is an international NGO founded in 1983 in Trieste, Italy by a distinguished group of scientists from the South under the leadership of the late Nobel laureate Abdus Salam of Pakistan. Its principal aim is to promote scientific excellence and capacity in the South for science-based sustainable development [83].

- Third World Organization for Women in Science **(**TWOWS**):** Established as an NGO in Trieste in 1989, TWOWS is the first international forum to unite eminent women scientists from the South with the objective of strengthening their role in the development process and promoting their representation in scientific and technological leadership [84].

- International Association of Science and Technology for Development **(**IASTED**):** A non-profit organization devoted to promoting economic and cultural advancement, IASTED was established in 1977. It organizes multidisciplinary conferences for academics and professionals, in both industrialized and developing countries, mainly in the fields of engineering, science, and education [85].

Perspectives on the nature of the development process itself have changed markedly during the last half-century. In the period of the 1950s–1970s, on the HIC side much of the development process was driven by and centered around post-colonial relationships and geopolitical cold-war maneuvrings, while LMICs themselves were beginning to seek ways to develop their own resources and capacities. There has been a movement away from HIC-driven approaches towards national self-determination and South–South cooperation and mutual reinforcement. Gradually there was a shift from a utilitarian perspective, which primarily focused on economic advancement as the main goal and saw human resources development, including S&T capacities, as a means of achieving this, to a human rights perspective which saw human development, equity and well-being as the primary objectives, with economic development being an important mechanism for enabling all people to achieve certain standards of health and freedom from want of basic needs as an inalienable right.

A series of world conferences in the 1990s, covering education, health, population, and sustainable development, culminated in the Millennium Declaration [86] in 2000. Reflecting the shifts in approach, the work of the Commission on Macroeconomics and Health, which reported to the World Health Organization in 2001, emphasized that health is an essential prerequisite for development, rather than the converse [87].

The role of science and innovation as drivers of development was examined in detail by the Task Force on Science, Technology and Innovation of the UN Millennium Project [47]. The Task Force, led by Calestous Juma and Lee Yee-Cheong, identified the important roles that science and technology can play in achieving the MDGs. It stressed the importance of S&T policies tailored to the specific needs and circumstances of each country and the need to create international partnerships that allow mutual learning.

The report of the Task Force outlined key areas for policy action, including:

- focusing on platform (generic) technologies
- improving infrastructure services as a foundation for technology
- improving higher education in science and engineering and redefining the role of universities
- promoting business activities in science, technology, and innovation
- improving the policy environment
- focusing on areas of underfunded research for development.

In a further study [88], Juma proposed that international development policy should be directed at building technical competence in developing countries rather than conventional relief activities. He argued that institutions of higher learning, especially universities, should have a direct role in helping to solve development challenges [89].

1.5
Chemistry and Development

Within the broader domain of S&T, chemistry has emerged as a key discipline able to contribute to development [90]. A number of NGOs, as well as programs within existing bodies, have been established to promote this contribution internationally. Two, in particular, are notable as examples of efforts at the global level to address major development needs and to build capacities for relevant chemistry in LMICs.

1.5.1
Chemical Research Applied to World Needs

At its meeting in Munich in 1973, the International Union of Pure and Applied Chemistry (IUPAC) considered ways in which it could foster opportunities for international cooperation. The result was the establishment of Chemical Research Applied to World Needs (CHEMRAWN) as a mechanism through which member nations of IUPAC could aid in identifying and solving important chemistry problems that have a direct impact on world needs [91]. The initial purposes proposed for CHEMRAWN were:

1) To identify human needs amenable to solution through chemistry with particular attention to those areas of global or multinational interest.
2) To serve as an international body and forum for the gathering, discussion, advancement and dissemination of chemical knowledge deemed useful for the improvement of humankind and our environment.
3) To serve as an international, nongovernmental source of advice for the benefit of governments and international agencies with respect to chemistry and its application to human needs.

The major activity of the CHEMRAWN Committee has been to organize a series of conferences, designed to identify and focus attention on world needs and to make recommendations for action to the global scientific community [92]. The highly ambitious nature of these conferences envisaged (Box 1.3) at the outset of CHEMRAWN illustrates the complexity and the importance of the potential roles of chemistry in development. In particular, four key elements remain the bedrock of achieving chemistry's potential in development almost four decades after the vision was first enunciated:

- A systems approach is essential to understanding and responding to human needs.
- Many interlocking systems are involved, requiring approaches that cross boundaries between S&T disciplines and social, economic, environmental and political sectors as well as needing engagement between governments, industries and academia.

Box 1.3 Chemical Research Applied to World Needs (CHEMRAWN)

"It was envisioned that CHEMRAWN activities would provide the basis for treating chemical-based human needs as systems. Thus, CHEMRAWN conferences by their very nature would be highly interdisciplinary and would take into account the social, economic, environmental and political factors, as well as the technical components involved. It was planned that these international conferences would attract world leaders from governments, industries and academia, and that the goal and focal point of the conference activities would be an attempt by recognized and influential world leaders to take an initial step toward developing a sense of future direction that would be of value to the world chemical community. Such direction would be provided in recommendations set forth in conference proceedings and made available to participants and policymakers and governments, industries, and academic institutions worldwide. Further, it was determined that CHEMRAWN conferences would provide continuity in areas where there is a persistent need."

Bryant Rossiter, first Chair of the CHEMRAWN Committee, quoted in [92].

- Engagement with politicians and the creation of a supportive policy environment are essential for advancing and sustaining the development agenda.
- All countries, including the less economically advanced, can contribute to the development process.

1.5.2
International Organization for Chemical Sciences in Development

The International Organization for Chemical Sciences in Development (IOCD) was the first international NGO specifically devoted to enhancing the role of the chemical sciences in the development process and involving chemists working in LMICs [93–96]. Its origins lay in a program established by the Special Programme of Research, Development and Research Training in Human Reproduction (HRP) at the World Health Organization (WHO) in the 1970s. Since many contraceptives appropriate for use in LMICs were not of major interest to the pharmaceutical companies whose markets were mainly in HICs, HRP-WHO sponsored a program to develop novel contraceptives outside the traditional pharmaceutical industry channels. In a project coordinated by the Belgian chemist Pierre Crabbé, the skills of groups of chemists in LMICs were engaged to synthesize compounds for biological evaluation. Over a number of years, several hundred novel steroids were synthesized, formulated and tested [97–99]. The success of this program [96] led to the idea that it might serve as a model for developing other drugs or even pesticides, while simultaneously stimulating capacity building in LMICs and enabling chemists in these countries to contribute to key S&T areas for development [100].

Building on this idea, Crabbé invited distinguished scientists from more than a dozen countries to meet at UNESCO, Paris in 1981, to consider how to give sustained support to the research work of chemists in developing countries. They recognized that many barriers hinder the efforts by scientists in LMICs to carry out research, including inadequate laboratory equipment, lack of up-to-date books and journals, long periods of isolation from mainstream scientific activities, and so on. The vision of how these barriers might be lowered was to engage scientists from LMICs in collaborative research with scientists from HICs. IOCD was established to take forward the model [101]. Initially housed at UNESCO in Paris, IOCD soon moved to Mexico City, where it was given support by the Ministry of Health. The first group of elected officers were Glenn Seaborg (Nobel Laureate chemist, Berkely University, USA) as President; C.N.R. Rao, (Head of the Indian Institute of Science, Bangalore, India) and Sune Bergström (Nobel Laureate chemist, Karolinska Institute, Sweden) as Vice Presidents; and Elkan Blout, (Dean of the Harvard School of Public Health, USA) also as a Vice President and Treasurer. The involvement of these eminent scientists and of a range of other high-profile scientists from LMICs and HICs in the IOCD Advisory Council (including the father of the "green revolution", Nobel Laureate Norman Borlaug), was important in the early years in securing funding from a range of international organizations and foundations and in attracting prominent scientists to serve as leaders of IOCD's scientific Working Groups (Figure 1.4).

The first two IOCD Working Groups were aimed at the development of compounds for male fertility regulation and to treat tropical diseases. Modest grants were provided to facilitate the purchase of laboratory supplies and support research students in the collaborating LMIC laboratories, with collaborators in HIC laboratories assisting to overcome barriers to supply and providing back-up such as advanced spectroscopic and analytical services. While the work inevitably proceeded slowly in the first few years, a key spin-off was the establishment of networks of chemists collaborating across countries and many of the contacts and collaborations survived long after the projects themselves came to an end. IOCD was able to sponsor a number of site visits and training exchanges and a key event was a meeting of all the scientists involved in the IOCD programs in Oaxtepec, Mexico in 1986.

Figure 1.4 IOCD scientists meeting at Berkeley, California in 1986. From left to right: Carlos Rius, IOCD's first secretary; Pierre Crabbé, founder; Elkan Blout, first treasurer and one of three founding vice presidents; Carl Djerassi, one of the inspirations behind IOCD; Sune Bergström, a founding vice president; Sydney Archer, leader of the Tropical Diseases Working Group; (unknown); Glenn Seaborg, IOCD's first president and associate director of the Lawrence Berkeley National Laboratory; C.N.R. Rao, a founding IOCD vice president; and Joseph Fried, leader of the Male Fertility Regulation Working Group. (Please find a color version of this figure in the color plates.)

Pierre Crabbé was tragically killed in a car accident in 1987, but under its new Executive Secretary, Robert Maybury, IOCD continued to work and to grow, adding additional working groups on plant chemistry and on environmental analytical chemistry, and later a group on bioprospecting. The emphasis has gradually shifted away from active project funding for chemistry research programs to capacity building activities through organizing training workshops, supporting attendance at scientific meetings and supporting the networking efforts of scientists in Africa. Most recently, IOCD has adopted two long-term projects to help reinforce scientific capacities in LMICs: one on Books for International Development, which organizes the collection and transfer of books and journals to developing countries, with each shipment containing tens of thousands of items; and one on micro-scale chemistry, which helps support an international program that provides low-cost, small-scale equipment to enable students to gain hands-on practical skills in experimental chemistry even in very resource-poor settings [101].

1.6
Science and Technology for National Development

1.6.1
Investments in Research and Development

From 2002 to 2007, world R&D expenditure increased by 44%, from an estimated 788.5 billion PPP$ (purchasing power parity dollars) to 1137.9 billion PPP$. In relative terms, 1.7% of the world's Gross Domestic Product (GDP) was devoted to R&D in 2007 [55]. A number of Asian economies, including those of the Republic of Korea, Taiwan, Hong Kong and Singapore, became highly successful during the last half century and were able to maintain growth rates of 8–10% over a number of years. While many factors have been considered to contribute to the success of these "Asian tigers", important common threads have been an emphasis on higher education and on balanced investments across a range of business and technology sectors. This has enabled the economies to grow rapidly and to shift away from dependence on the export of raw materials and primary products, towards the production of high value-added products of S&T.

Given the importance of S&T for economic advancement and competitiveness in all countries [102], it is not surprising that, in recent years, there has been an increased focus on targeting specific levels of national investment in research and development (R&D) as a key driver of innovation. In 2002, the European Union (EU) set a target of reaching a level of 3% gross expenditure on R&D (GERD: also known as "research intensity") as a percentage of GDP by 2010. Of this 3%, it was projected that one third would come from public sector investment and two thirds from the private sector. By 2007, only Finland and Sweden had passed the 3% target, Austria, Denmark and Germany had reached 2.5% and France had reached 2%, while ten of the 27 EU member states were still investing below 1% [103, 104] (Figure 1.5a).

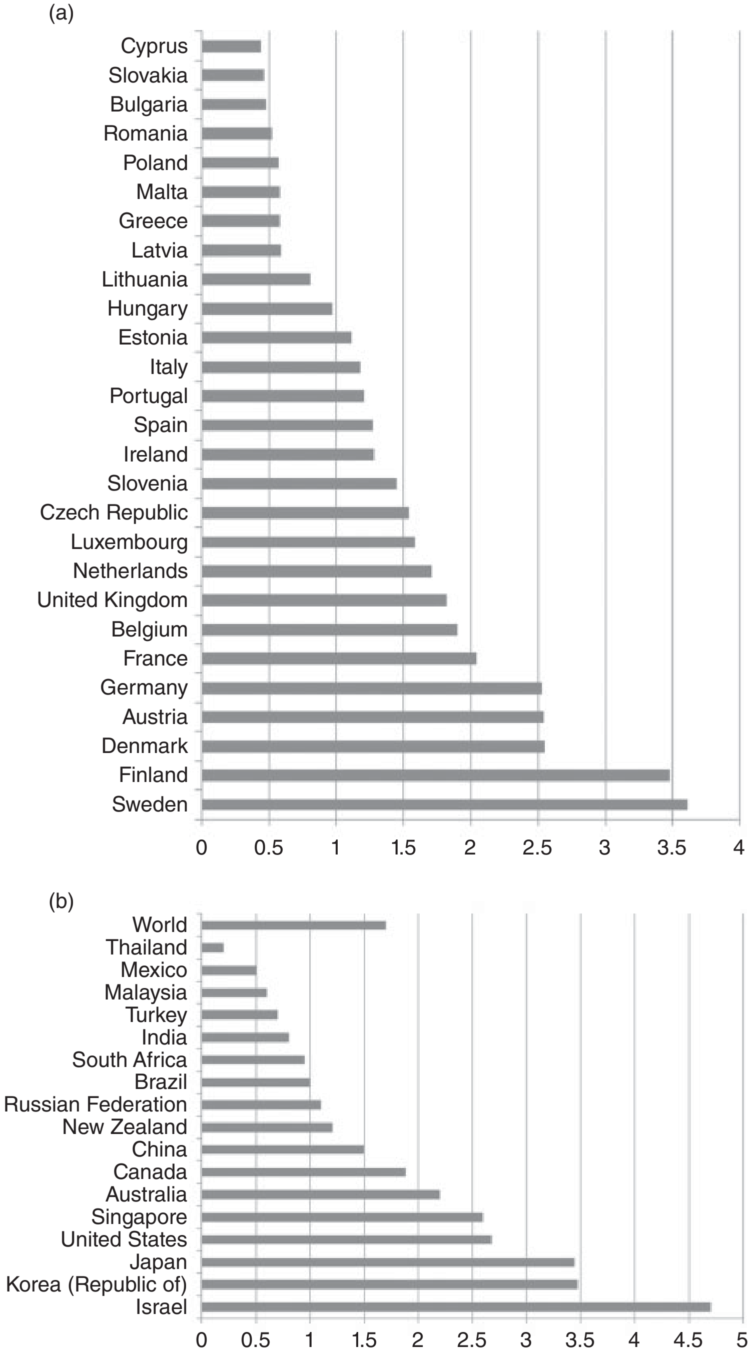
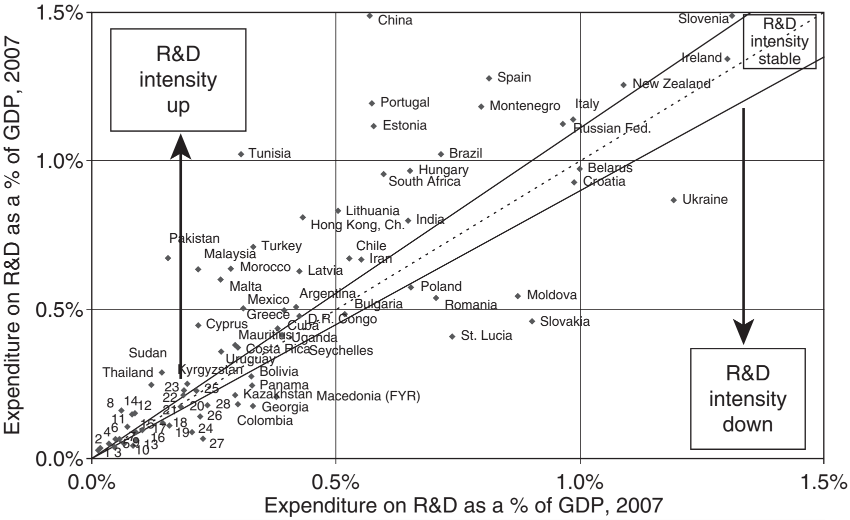


Figure 1.5 Gross domestic expenditure on R&D as a percentage of GDP for 2007. (a) European Union countries (data from [104]), (b) other countries (data from [104]).

Outside the European Union, gross expenditure on R&D among economically advanced countries and emerging economies also varies widely (Figure 1.5b):

- Recognizing the weakness of its performance in science, technology and innovation, the African Union (AU) has initiated efforts to increase its investments in R&D, spearheaded by the New Partnership for Africa's Development (NEPAD). At the first NEPAD Ministerial Conference on Science and Technology in November 2003, Ministers of Science and Technology of 20 AU countries reaffirmed their commitment to increasing public spending on R&D to at least 1% of GDP within five years and the AU commitment to this 1% target has been reiterated on a number of occasions and member countries are still working towards it [103, 105]. To date, only South Africa regularly measures and reports data on its research intensity, which had risen to 0.95% by 2007 – of which 56% came from the business enterprise sector [106]. Data on R&D investments in other African countries appears only sporadically and, for the few countries where information is available, suggests a range from <0.1% (Algeria) to 1% (Tunisia) in North Africa and 0.5% (Mozambique) or less in the rest of Africa. *Africa's Science and Technology Consolidated Plan of Action 2006-2010* was first elaborated in 2005 by the African Union/NEPAD and is being implemented with assistance from UNESCO, which has adopted three flagship projects: (i) capacity building in S&T and innovation policy; (ii) enhancing science and technology education; and (iii) the African Virtual Campus. NEPAD has instituted the African Science, Technology & Innovation Indicators Initiative (ASTII) and the establishment of the African Observatory for Science, Technology and Innovation (AOSTI). ASTII aims at the development and adoption of African common science, technology and innovation indicators, while AOSTI will ensure that the STI indicators and information gathering as well as collation, compilation and validation are standardized [107].
- Among the emerging economies, China has demonstrated a dramatic rate of increase in GERD, which almost tripled to 1.5% between 1996 and 2007 [55] (Figure 1.6).
- Israel, Japan and Korea all invest more than 3% of GDP in R&D. The USA has long recognized the strategic economic importance of investing in R&D but its research intensity has not kept pace with this leading group. In April 2009, President Barack Obama announced that the USA will devote more than 3% of its GDP to R&D, with policies that invest in basic and applied research, create new incentives for private innovation, promote breakthroughs in energy and medicine, and improve education in math and science. This represents the largest commitment to scientific research and innovation in American history [108].

The term "Innovative Developing Countries" (IDCs) has begun to be used to describe a number of countries which have been making strong advances in strengthening their S&T to support their own development. These include Argentina, Brazil, China, India, Indonesia, Malaysia, South Africa and Thailand. At a



Note: countries in the left-bottom comer of the graph are represented by the following numbers.
1: Zambia; 2:Brunei; 3: Bosnia & Herzegovina; 4: Guatemala; 5: Honduras; 6: Lesotho; 7: Jamaica; 8: Myanmar; 9: Saudi Arabia; 10: Indonesia; 11: Macao, Ch.; 12: Peru; 13: Nicaragua; 14: Ecuador; 15: Paraguay; 16: Tajikistan; 17: Trinidad & Tobago, 18: Philippines; 19 Burkina Faso; 20: Ethiopia; 21: Sri Lanka; 22: Armenia; 23: Mongolia; 24: Kuwait; 25: Egypt; 26: Madagascar; 27: Algeria; 28: Azerbaijan.

Figure 1.6 Changes in R&D intensity, 1996–2007.

meeting in 2005 to mark the 60th anniversary of South Africa's Council for Scientific and Industrial Research, leaders of science institutions from a number of these IDCs reached a consensus [109] on finding ways for S&T to play a part in sustainable development (Box 1.4). Some of the IDCs are now becoming significant development assistance partners, especially in Africa, including providing support for building higher education and research capacity [110].

1.6.2
Outputs from Investments in Research and Development

Not surprisingly, the higher levels of investments in R&D seen in many of the HICs and emerging economies correlate, at least to a degree, with science, technology and innovation outputs.

In particular, there is a strong correlation between levels of R&D investments and the densities of research workers [55] (Figure 1.7). For example, Asia represented 41.4% of world researchers in 2007 compared to 35.7% in 2002. This rise was mainly due to the increasing share of researchers in China from 14.0% to 20.1% between 2002 and 2007, reflecting the major increase in China's investments in R&D.

More funding and more researchers generally lead to higher outputs of scientific papers (Figure 1.8). The countries of the European Union, the United States and Japan collectively represent almost 70% of global R&D expenditure and these

Box 1.4 The Tshwane Consensus on Science and Development

The Emergence of Innovative Developing Countries (IDCs)

Many challenges remain. The world needs new and sustainable energy sources, protection from emerging diseases, and lower cost infrastructure. Moreover, the S&T environment has changed significantly in the last ten years. Knowledge production has been internationalized, access to money and skills has become increasingly competitive, and global technology and markets are changing with breathtaking speed.

A new set of actors has emerged in the quest to meet these challenges. Following sustained investment in education, research infrastructure and manufacturing in a number of developing countries, the IDCs have achieved high levels of economic progress and overall improvements in human wellbeing. How can these successes be generalized, and what role do the IDCs have in contributing to sustainable development?

The S&T leaders concluded that the IDCs can play a crucial role in developing innovative and appropriate solutions to global challenges, and at the same time strengthening their own S&T expertise. These leaders urged IDCs to coordinate their efforts, in order to increase investment in S&T aimed at the problems of developing countries. In particular, the leaders stressed the need for:

- developing nations, especially the poorest, to devote a proportion of their resources to S&T
- S&T leadership in developing countries to be strengthened and to define a clear set of priorities; this leadership needs to make a persuasive statement to the public that the scientific effort is essential and useful
- the political leadership of developing countries to press for a greater role in decision making on global development programs, including bilateral and multilateral aid; and to insist that a proportion of these resources be devoted to research and nurturing local scientific and technical capacity
- the benefits of S&T need to be extended to all; S&T efforts need to be increasingly directed to the creation of affordable and accessible products and services for poor people
- the strengthening of mechanisms, such as academies of S&T, for advising high levels of government on issues of S&T
- access to careers in S&T to be widened, and at the same time systems that reward and offer S&T careers to the most talented to be developed
- the broadening of the science education base within schools, technical colleges, universities, science councils, academies of sciences, government departments and industry; these institutions are fundamental to development and wealth creation. It is clear that an environment of excellent research is necessary to attract and retain young talent in scientific careers.

Although it is highly desirable for all countries, and especially developing countries to have functioning S&T systems, the symposium noted that this is not presently the situation, and in the interim several steps needs to be taken, including:

- the establishment of regional networks between national systems to overcome the lack of a critical mass, which is presently limiting the success of S&T in many developing countries
- the implementation of appropriate performance measures at all levels and for different types of S&T institutions in order to get the most out of the available resources

- the introduction of appropriate tax incentives and grants to encourage private sector participation in R&D; additional private sector resources for S&T could be accessed by addressing sources of market failure, including the preconditions for the entry of Technology Risk Capital.
- the close networking of universities, research councils and industry in order to promote innovation, entrepreneurship and wealth generation; mission-oriented clusters of institutions focused on identified priority issues must be established to aim at discovery, development and delivery.

In conclusion, the leaders noted that it is time for a number of important initiatives. It is time for developing and post-colonial societies to "name the ghosts" of science, technology, and higher education. While benefiting many people, S&T has also systematically excluded many groups. Governments and industries often use technologies in a way that harms both workers and the natural environment. Openness about these spectres will help to assure more equitable and constructive practices in the future.

It is also time for the IDCs to act collectively and think globally. An effective response to a number of shared global challenges, such as global climate change, infectious diseases and the loss of biodiversity, can only be achieved with the involvement of all countries, and especially the developing countries. The S&T systems of the innovative developing countries can play a crucial role in building such national capacity, and in shaping their own futures.

Extract from Tshwane Consensus [109]

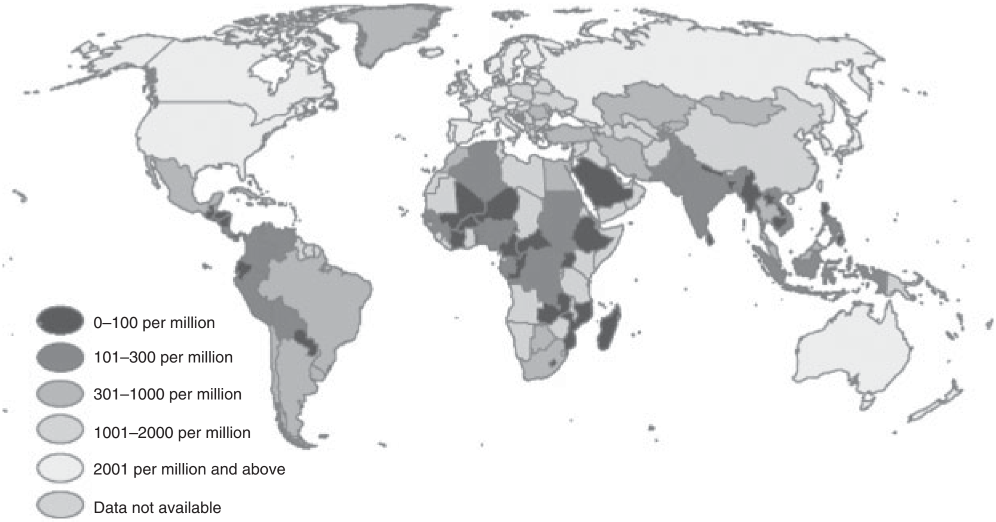


Figure 1.7 Researchers per million inhabitants, 2007 or latest available year. (Please find a color version of this figure in the color plates.)

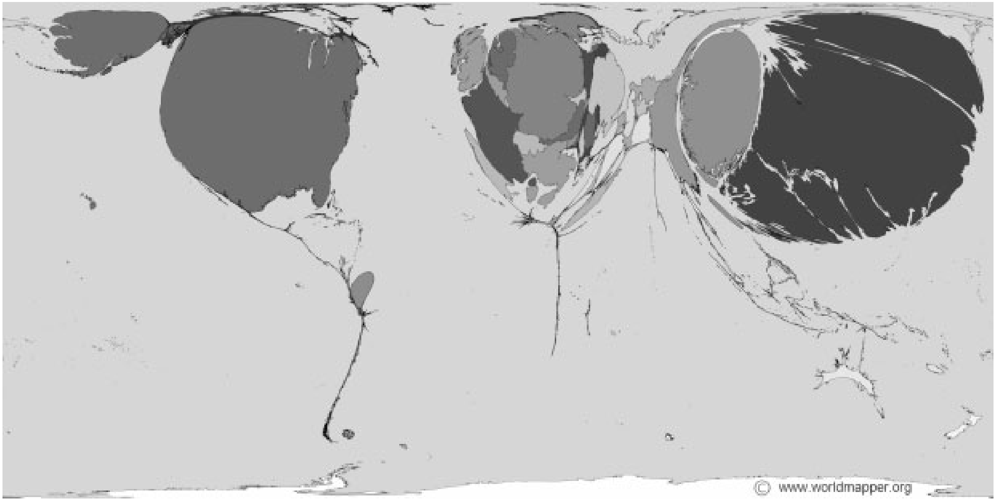


Figure 1.8 Scientific publications by countries, 2001. Territory size shows the proportion of all scientific papers published in 2001 written by authors living there. Scientific papers cover physics, biology, chemistry, mathematics, clinical medicine, biomedical research, engineering, technology, and earth and space sciences [111]. (Please find a color version of this figure in the color plates.)

countries publish roughly three times more scientific papers per person living there than in any other region [55, 111]. Bibliometric analyses of country outputs can be a useful tool for uncovering strengths and weaknesses in particular areas of science [112, 113]. For example, a 2003 study [114] in Malaysia noted that more papers were produced by Malaysian scientists in physical chemistry (10.16% of the total) than in any other area of science between 1955 and 2002, followed by agriculture (5.14% of the total).

The largest outputs of patents are predominantly made by HICs [111] (Figure 1.9). In 2002, 312 000 patents were granted around the world. More than a third of these were granted in Japan and just under a third were granted in the United States.

Migration of highly skilled workers ("brain drain") has a powerful effect on these outputs. The loss of such workers from the LMICs substantially lowers their capacities to innovate. One study [115] of migration identified 15 countries, especially in the Latin America/Caribbean and African regions, for which the percentage of highly skilled workers among the migrants was in the range 33–83% (Figure 1.10).

Migrants can bring a range of economic benefits to the receiving countries, including higher rates of innovation. Productivity gains in a number of destination places have been traced to the contributions of foreign students and scientists to the knowledge base. Data from the USA show that between 1950 and 2000, skilled migrants boosted innovation: a 1.3% increase in the share of migrant university graduates increased the number of patents issued per capita by a massive 15%, with marked contributions from science and engineering graduates and without any adverse effects on the innovative activity of local people [116, 117].

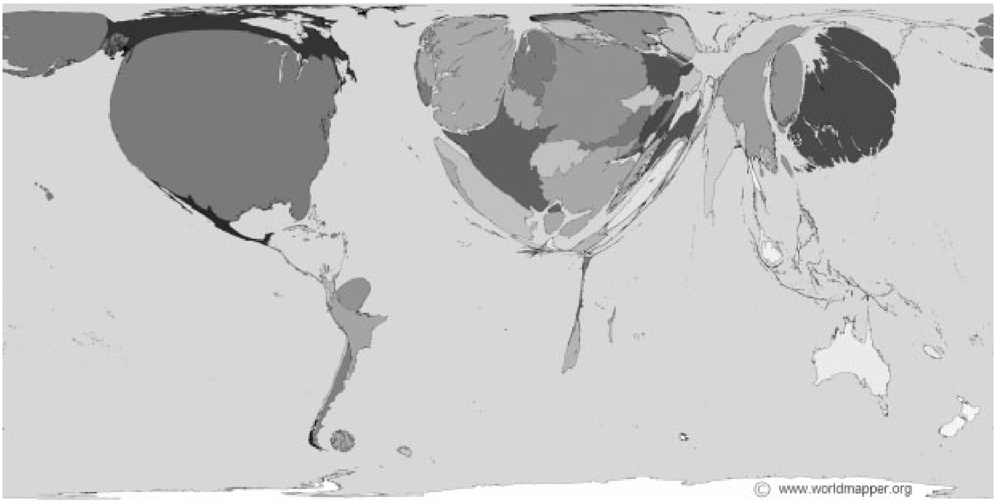


Figure 1.9 Patents granted by countries, 2002. Territory size shows the proportion of all patents worldwide that were granted there [111]. (Please find a color version of this figure in the color plates.)

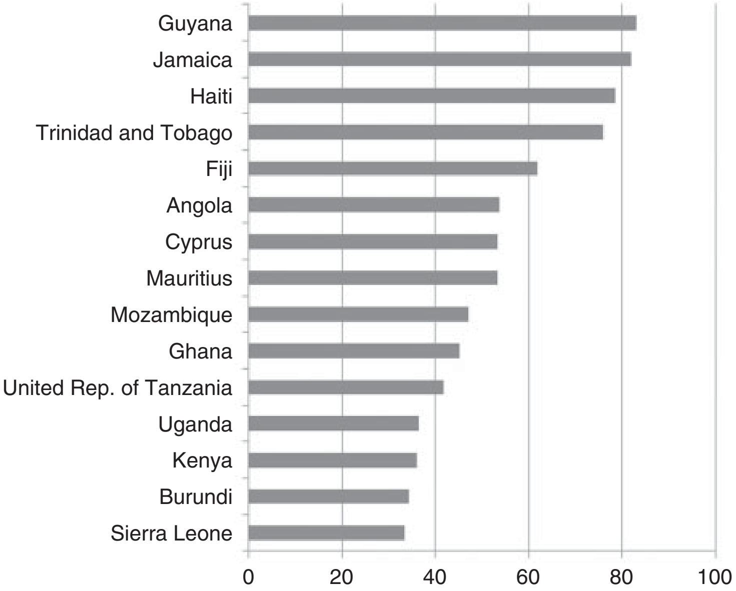


Figure 1.10 Percentages of highly skilled expatriates among total expatriates from selected non-OECD countries.

1.6.3

Connecting Science, Technology and Innovation

Scientific output in the form of publications and patents does not necessarily translate directly into innovation. The innovation environment in which scientists, inventors and entrepreneurs work plays a substantial role in determining how successful a country becomes in translating novel ideas into practical processes and products that contribute to national development [118].

A Rand study [119] which examined the scientific capability of 29 representative countries to adopt 16 technology applications divided the countries into four capability categories:

- **Advanced –** Australia, Canada, Germany, Israel, Japan, Korea, USA
- **Proficient –** China, India, Poland, Russia
- **Developing –** Brazil, Chile, Colombia, Indonesia, Mexico, South Africa, Turkey,
- **Lagging –** Cameroon, Chad, Dominican Republic, Egypt, Fiji, Georgia, Iran, Jordan, Kenya, Nepal, Pakistan

The study identified a number of major drivers and barriers to the capacity to adopt technological innovation:

- Cost and financing
- Laws and policies
- Social values, public opinion, and politics
- Infrastructure
- Privacy concerns
- Use of resources and environmental health
- R&D investment
- Education and literacy
- Population and demographics

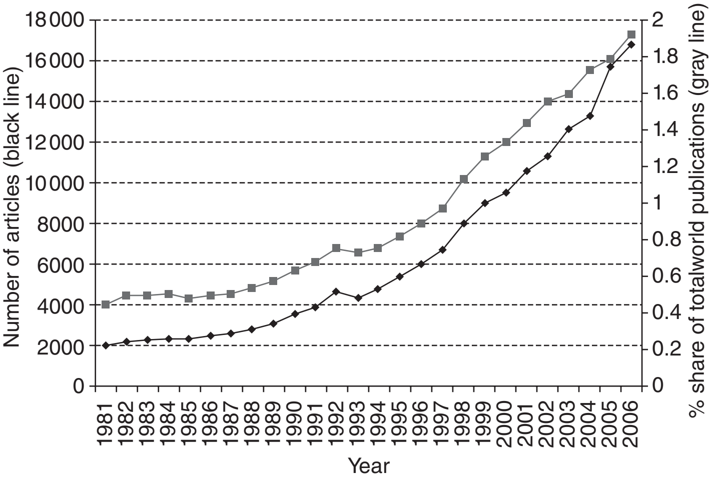
Clearly, therefore, countries need to do more than providing support for the pursuit of S&T if they wish to reap the economic and development benefits. Investments in science, including chemistry, must be coupled with national policies on the applications of science and creation of national environments that foster innovation. Brazil provides an example of a country that is pursuing this approach (Box 1.5) [120–125]. Areas now receiving considerable attention, which have a chemistry linkage, include bio-fuels and pharmaceuticals.

Among the emerging economies, China has demonstrated an extremely high growth rate in recent years, coupled with accelerated investments in R&D (Figure 1.6). An important aspect of China's development has been the capacity to take a long-term approach to investment and planning. It is remarkable that, in 2008, the Chinese Academy of Sciences published a 50-year science strategy as an extension to the Mid-to-Long-Term Plan for Development of Science and Technology (2006–2020) issued by the State Council of China [126].

While India's overall investment in S&T has lagged behind those of other emerging economies such as Brazil, China and South Africa, nevertheless, it

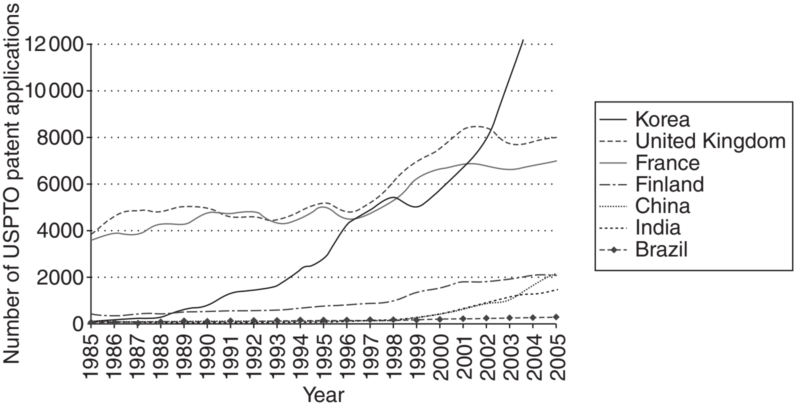
Box 1.5 Brazil's experience of promoting of science, technology and innovation (ST&I)

Brazil began systematically investing in S&T in the early 1950s, establishing national councils for research and for postgraduate education. During the military rule period (1964–1985), the funding system was consolidated with the creation of agencies for innovation and S&T; and a 1988 law required Brazil's states to create S&T funds. Following a serious health crisis in the 1980s, much greater attention began to be given to S&T to solve national problems and increased investment was soon followed by increasing scientific output.



Brazilian SCIE-indexed publications, total and share of world output, 1981–2006.

However, the environment for innovation remained unfavorable with laws that restricted the ability of university-based researchers to develop their discoveries. As a result, Brazil lagged behind other economies with a more open approach.



US Patent and Trademark Office patent applications, Brazil and selected countries, 1985–2005.

Continued

Brazil has taken some key steps to improve the environment for S&T and innovation:

- Sixteen Sectoral Funds were created between 1998 and 2008. They direct a fraction of the taxation of key industries to R&D projects to focus sector-specific research collaborations between enterprise, universities and research institutions, as well as to ensure the redistribution of research resources to help build capacity in less developed regions of the country.
- A new Innovation Law was adopted in 2004, to stimulate research innovation and remove barriers making it difficult for public sector researchers and private companies to collaborate.
- Brazil has significantly increased its investment in R&D in recent years, aiming to raise it from a level of around 1% of GDP to 1.5% by 2010 and with a prospect of increasing to 2% by 2020.
- Very importantly, the improved legal frameworks, investments and economic policies have been complemented in recent years by strong political will that recognizes that ST&I are at the center of economic development and social transformation.

See [120].

established a strong position in a number of chemistry-related fields. In particular, prior to accession to the World Trade Organization (WTO) in 2005 [127], India's non-recognition of product patents and innovative use of "reverse engineering" enabled it to establish itself as the "world's pharmacy", becoming the largest source of generic pharmaceuticals for other LMICs [128]. Having joined the WTO, the India pharmaceutical industry is being strongly encouraged to innovate and create its own intellectual property.

1.7
Capacity Building: Some Key Requirements for Chemistry's Role in Development

1.7.1
Evolution of Capacity Building Approaches in LMICs

Over the last few decades, the approach to capacity building in LMICs has evolved through several distinct stages [129]. Initially, the focus was on training of individual chemists – mainly by supporting students from LMICs to attend universities in HICs to obtain higher degrees and research experience. However, the graduates often found it difficult to pursue science careers on returning home and were frustrated by the lack of suitable laboratories, chemicals and equipment to follow their research interests. Some were assisted by maintaining close relationships with the HIC institutions where they had trained and by developing new North–South and South–South networks. Later, a more systematic effort emerged to develop high quality centers of advanced teaching and research in LMICs, creating their own cohorts of masters and PhD graduates and providing support and positions for those returning from advanced training abroad. However, chemistry and other academic disciplines have generally continued to have low esteem in many LMICs and to lack rewarding career pathways able to retain the brightest people. The importance of basic sciences like chemistry has been the subject of major emphasis in a number of conferences attended by scientists, policy makers and donor representatives [130, 131].

In the light of this mixed history of progress, but reflecting the strengthening recognition of the important roles that chemistry and other sciences need to play in the process of development, attention has turned, more recently, to addressing the entire system of teaching and research in a more comprehensive way.

Chemistry is taught within the overall framework of secondary and higher education. In many countries there are fragmented systems, sometimes involving separate ministries. Public sector teachers and lecturers in LMICs are often employed directly by the state as civil servants and subjected to a wide range of government regulations affecting salaries and terms and conditions of employment. Research is typically funded through a diverse and complex array of channels, including general university funding bodies, science councils and specific ministry programs and may involve federal, state and city-based sources and earmarked taxes. The private sector has developed some role in teaching, with many LMICs having private universities, but relatively little academic research is funded from private sources in these countries and few LMIC private universities have significant research capacity. On the other hand, overseas funding for research in LMICs may seem extremely large relative to national sources. The complex interplay of all these factors makes it difficult for a country to plan the growth and development of disciplines like chemistry and to enhance the roles that they play in addressing national priorities.

A further issue is that many scientists are resistant to the very notion of national planning, fearing that the identification of national priority areas for research will lead to the elimination of "blue skies research" and a corresponding loss of "academic freedom". An open public debate is needed which avoids taking an all-or-nothing extreme view about the direction of resources, but focuses on what are the appropriate proportions of national resources that should be apportioned to priority-focused versus undirected research and appropriate and evidence-informed mechanisms for selecting the priorities. Scientists in LMICs need to work more closely with their political leaders to show the importance of investment in long-term research in science. They are often very quick to blame their leaders for not allocating funds for research, especially when they wish to appeal for funding from external agencies.

1.7.2
National Policies for S&T

The evidence from emerging economies such as those in Brazil and China indicates that science and scientists fare well and make positive contributions to development when there are in place:

- National policies for science, technology & innovation, addressing
  - S&T education and training
  - financing national R&D
  - stimulation of innovation
  - exploitation of natural resources
  - environmental protection
  - regulation of medicines
  - regulation of intellectual property
- Key infrastructures for
  - education
  - R&D
  - innovation

Taiwan provides an example of a country which transformed its economy during the second half of the 20th century, with national planning and investment in chemistry capacity playing a key role (Box 1.6) [132].

1.7.3
Responsibilities

The government needs to take responsibility for instituting comprehensive policies for S&T, increasing levels of investment of public funds in R&D and fostering an environment that values knowledge and evidence and that promotes innovation. The scientists and academics have a corresponding set of responsibilities to be sensitive to national priority problems and to the need to communicate effectively with policy makers. The development of mutual trust and improved understanding between policy makers and researchers is now the subject of considerable attention – especially in areas such as health and the environment – and chemists must also engage in order to influence and benefit from the process.

It is also vital for international development partners to accept and orient their behavior towards the systems-based approach. Development assistance has undergone a revolution in recent years, with the preferred modality shifting away from project-based bilateral programs. Many such programs are now perceived to have had limited success and poor sustainability, being too donor-driven and failing to build country capacities and local support. In their place have come new multilateral arrangements based on sector-wide programs or general budget support, enabling the government to be in the driving seat in terms of national policies and fostering the building of government capacities for policy development, implementation and accountability. This new model has been formalized in the Paris Declaration on Aid Effectiveness and Accra Agenda for Action (Box 1.7) [133].

However, while the Paris/Accra principles are increasingly being applied to broad areas of development assistance to social and economic sectors and overall government finances, the entire field of research has been relatively neglected. Northern research institutions, research funding agencies and development assistance partners often still indulge in project-type approaches that engage individuals

Box 1.6 Taiwan's experience in national planning and investment in chemistry capacity

Taiwan's "economic miracle"

Taiwan's per capita GNP rose from US$919 in the 1950s, through US$1671 in the 1960s, US$3626 in the 1970s and US$6501 in the 1980s to US$7358 in 1990, as the agrarian economy was transformed into an export-oriented industrial one. In 1990, the total value of industrial production was US$165.3 billion, giving Taiwan foreign reserves of US$80 billion (first or second in the world).

By the early 1990s, the chemical industry was the largest industrial sector, contributing 24.2% of the total production value of US$165.3 billion, but only 8.5% directly to export sales of US$95.6 billion. This demonstrates the strategic importance of the chemical industry, as a supplier of materials and chemicals, in underpinning other export industries, including electrical/electronic goods and textiles.

The development of Taiwan's chemical industry can be divided into a number of phases:

1913–1943 Manufacturing of basic chemicals (e.g., fertilizer, chloralkali) (Japanese colony)

1944–1953 Production of substitutes for imported consumer goods (e.g., consumer commodities, agricultural products)

1954–1967 Development of light industries (emphasizing paper/food/textile products, etc)

1968–1975 Beginning of backward integration of petrochemical industry (boosting the export of textile products)

1976–1988 No. 3 and No. 4 naphtha crackers started with the fastest growth of the petrochemical industry

1989 Restructured strategy to shift away from commodities to higher value chemical products and advanced materials

Four main factors contributed to Taiwan's success in becoming one of the world's leading producers of a number of plastics and synthetic fibers by the 1990s:

1) Establishing an integrated chemical industry – for example, integrating backwards from a garment industry dependent on cheap labor and raw materials by successively developing capabilities for the synthesis of earlier intermediates (terylene: ethylene glycol, terephthalic acid: ethylene, xylene); similarly the shoe industry was strengthened by development of the plastics industry.

2) Development of a "debottle-necking" capacity – creating a cadre of skilled engineers and technicians able to de-bug and even improve on technology (e.g., for vinyl chloride production) originally imported from elsewhere.

3) Cooperation between up/mid/downstream operators for example, in the pricing of chemical raw materials, intermediates and products to ensure competitiveness.

4) Strong support by the government – including tax and investment incentives, well planned industrial zones, government-owned low-profit raw material and intermediate manufacturers and production/procurement agreement between these and petrochemical suppliers, custom/tariff protection and export incentives.

Information from [132]

Box 1.7 Paris Declaration on Aid Effectiveness and Accra Agenda for Action

The Paris Declaration, endorsed on 2 March 2005, is an international agreement to which over 100 Ministers, Heads of Agencies and other Senior Officials adhered and committed their countries and organizations to continue to increase efforts in harmonization, alignment and managing aid for results with a set of monitorable actions and indicators. Key principles are:

Ownership Partner countries set their own strategies for poverty reduction, improve their institutions and tackle corruption.

Alignment Donor countries align behind these objectives and use local systems.

Harmonization Donor countries coordinate, simplify procedures and share information to avoid duplication.

Results Partner countries and donors shift focus to development results and results get measured.

Mutual accountability Donors and partners are accountable for development results

The Accra Agenda for Action was drawn up in 2008 and builds on the commitments agreed in the Paris Declaration, focusing on:

Predictability Donors will provide 3–5 year forward information on their planned aid to partner countries.

Country systems Partner country systems will be used to deliver aid as the first option, rather than donor systems.

Conditionality Donors will switch from reliance on prescriptive conditions about how and when aid money is spent to conditions based on the partner country's own development objectives.

Untying Donors will relax restrictions that prevent partner countries from buying the goods and services they need from whomever and wherever they can get the best quality at the lowest price.

Based on [133].

or institutions in specific research or capacity-building programs. These not only ignore but often effectively undermine any existing national policies and programs, drawing scarce research resources into externally-driven activities. The Australian Centre for International Agricultural Research provides an example of an international research program that is shaped for congruence with the Paris/Accra principles [134]

Chemists in LMICs can help to counter these fragmentary approaches by engaging – among themselves, with science colleagues and with policy makers – in serious analysis and debate to promote the establishment of clear national policies on S&T and to support their governments to encourage HIC collaborators and development assistance partners to harmonize their approaches and work through and in alignment with the national policies.

1.7.4
Professional Associations and Cooperative Networks for Chemistry and Development

Professional associations such as national societies for chemistry or its subbranches played an important role in facilitating the development of the subject and the profession in countries industrializing in the 19th and early 20th centuries. Through their impact on training, professional qualifications, the dissemination of information, encouraging good standards of practice, and the popularization of science, they contributed to strengthening the roles and contributions of chemistry in enhancing knowledge, wealth and health in these countries.

The world's largest professional society for chemistry is the American Chemical Society, founded in 1876 and now having over 160 000 members [135]. The Royal Society of Chemistry (RSC) [136] the largest organization in Europe for advancing the chemical sciences, was formed in 1980 by amalgamation of the Chemical Society (founded 1841); the Society for Analytical Chemistry (founded 1874, initially as the Society of Public Analysts); the Royal Institute of Chemistry (founded 1877, initially as the Institute of Chemistry of Great Britain) and the Faraday Society (founded 1903). Other early chemical societies include Australia (1917) [137], Austria (1897) [138], Brazil 1922 [139], Egypt (1928) [140], France (1901) [141], Germany (1867) [142], Japan (1878) [143], Netherlands (1903) [144], Norway (1893) [145], Portugal (1911) [146], Russia (1868) [147], South Africa (1912) [66], Spain (1903) [148], Sweden (1883) [149] and Switzerland (1901) [150].

The International Union of Pure and Applied Chemistry (IUPAC), founded in 1919, includes many national chemical societies among its members and provides global networking opportunities through its conferences and symposia [151]. Recently, international groupings of chemical societies have taken on regional networking and capacity building roles. For example:

- European Association for Chemical and Molecular Sciences – multiple society members from 37 European countries [152]
- Federation of African Societies of Chemistry (FASC) – established in 2006 with assistance from the Royal Society of Chemistry, it has 8 member societies, one of which is the West African Chemical Society (representing members from Benin, Burkina Faso, Côte d'Ivoire, Guinea, Mali, Niger, Senegal, Togo) [153].
- Federation of Asian Chemical Societies – 28 member chemical societies in the Asia-Pacific region [154].

In an example of inter-regional collaboration, FASC participated in launching the Pan African Chemistry Network (PACN). This is a program for Africa launched in November 2007 by the Royal Society of Chemistry with support from Syngenta. The PACN has established initial hubs in Nairobi and Addis Ababa and aims to help African countries to integrate into regional, national and international scientific networks [155].

One of the important ways that chemists can contribute to sustainable capacity development and utilization in LMICs is by developing and participating in South–South and North–South–South cooperation networks. During the course of the last century, advances in science generally have moved from being the work of highly gifted individuals (e.g., Galileo, Newton, Darwin, Einstein) to involving the work of localized groups of collaborators (e.g., Watson and Crick) and then to international networks of scientists. Such networks are not only a feature of "big" science such as particle physics or the human genome project, where dozens or hundreds of collaborators may be involved at a large number of centers, but also extend to a range of projects which are substantial scientific challenges that require a critical mass of workers tackling different aspects of a problem and/or that cross disciplinary boundaries [156, 157].

In addition to these types of networks that are driven by the demands of tackling large, complex challenges, there are also networks whose purpose is to provide support and capacity building for scientists working in settings with limited resources.

Both types of networks are of relevance to many chemists working in LMICs, since they provide opportunities for being associated with large, cutting-edge global programs as well as enabling research to be conducted in areas of local interest or relevance and reducing researchers' isolation [158]. There are recent trends showing the increasing engagement of chemists in networks aiming to foster research, capacity building and development, as summarized below.

The International Science Programme (ISP) at Uppsala University supports networks on a long-term basis. It aims at assisting developing countries to strengthen their domestic research capacity within the chemical, physical and mathematical sciences. Support focuses on regional networks and on research groups that are primarily in least developed countries targeted by the Swedish government for long-term cooperation [159].

The International Foundation for Science (IFS) receives funding from governmental and nongovernmental sources, as well as national and international organizations and has an annual budget of approximately US$ 5 million. A primary form of support provided is in the form of an IFS Research Grant to young scientists at the beginning of their research careers, which amounts to US$ 12 000 and may be renewed twice. It is intended for the purchase of the basic tools needed to conduct a research project: equipment, expendable supplies, and literature. Since 1974 there have been 3500 IFS Grantees in Africa, Asia and the Pacific, and Latin America and the Caribbean. Of these 22% are women. IFS also acts as both enabler of existing and emerging networks and convener of new ones. Involvement is especially in the initial stages, with IFS providing seed money, co-operative and administrative assistance and funding to workshops, training courses, exchange visits and fellowship programs [160]. Examples of IFS-and ISP-supported networks active in chemistry include:

- AFASSA (Co-ordination of Networks for Research on Biological Resources in Africa, Asia and South America) [161]

  AFASSA was set up as a result of an international symposium on natural product research held in Montevideo, Uruguay, in 1999, with participating scientists from Africa, Asia and South America. Members to date are:
  - African Laboratory of Natural Products
  - Asian Network of Research on Anti-diabetic Plants
  - Latin American Network for Research on Bioactive Natural Compounds
  - Network for Analytical and Bio-assay Services in Africa
  - Natural Products Research Network for Eastern and Central Africa

  - Southern African Regional Co-operation in Biochemistry, Molecular Biology and Biotechnology

- ANCAP (African Network for the Chemical Analysis of Pesticides) [162]
  ANCAP was initiated in 2001 under IFS auspices. Member countries are to date Ethiopia, Kenya, Tanzania and Uganda.

- NABSA (Network for Analytical and Bio-assay Services in Africa) [163]
  See below. IFS and NABSA work on the issue of maintaining proper function of scientific equipment.

- NAPRECA (Natural Products Research Network for Eastern and Central Africa) [164]
  NAPRECA was initiated in 1984. Among the founding African scientists were several IFS grantees. In 1987, NAPRECA became affiliated to UNESCO as one of UNESCO's network programs. IFS continues to provide funding for specific projects. NAPRECA members are mainly chemists, but also biologists and pharmacologists, working on the chemistry, botany, biological activities and economic exploitation of natural products. The NAPRECA headquarters is located in Dar es Salaam, Tanzania, and there are local branches in nine countries (Botswana, DR Congo, Ethiopia, Kenya, Madagascar, Rwanda, Sudan, Uganda, Zimbabwe).

- NITUB (Network of Instrument Technical Personnel and User Scientists of Bangladesh) [165]
  NITUB was formed in 1994 with seed money from IFS. The main objective of NITUB is to improve the competence of scientists and technical personnel to operate, maintain, and repair scientific instruments. NITUB maintains an inventory of scientific instruments at Bangladeshi institutions, and aims to create a stock of spare parts. The General Secretary is located in the Department of Chemistry, University of Dhaka.

- NUSESA (Network of Users of Scientific Equipment in Southern and Eastern Africa) [166]
  NUSESA was initiated in 1989 with the aim to provide a forum for information and discussion on issues related to the purchase, use, and maintenance of scientific equipment in southern Africa. IFS passed on the coordination and administration of NUSESA activities when the NUSESA Secretariat was established in 1996 in Harare, Zimbabwe. Since NUSESA has secured funding from government agencies, IFS–NUSESA joint collaboration has evolved to policy-making and consultation. Local NUSESA chapters have been set up in 16 countries (Botswana, Eritrea, Ethiopia, Kenya, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe). The NUSESA Secretariat is located at University of Western Cape in South Africa.

- WANNPRES (Western Africa Network of Natural Products Research Scientists) [167]

> WANNPRES was established in 2002 by COSTED (Committee on Science and Technology in Developing Countries) on the initiative of a group of scientists from universities and research institutes in West Africa. The objective with WANNPRES activities is to enhance research and capacity building in the conservation and effective use of natural resources in Africa. IFS involvement dates back to the founding assembly. The WANNPRES Secretariat is located at the Department of Chemistry at the University of Ghana.

In the area of providing support and capacity building for scientists working in settings with limited resources, IOCD [102] began a program in the 1980s to provide analytical services for chemists in LMICs. This was initially a North–South network, with chemists at City University, London (Stephen Matlin), the University of Missouri (Michael Tempesta) and the Universidad Nacional Autónoma de México (Carlos Rius) receiving samples from chemists in a range of countries in Africa, Asia and Latin America and providing, free of charge, infrared, ultraviolet, NMR and mass spectra. In some cases, at the invitation of the submitting group, assistance was provided with the interpretation of spectra and the elucidation of structures of synthetic and natural products.

In 1992, IOCD's Walter Benson participated in a meeting in Gaborone, Botswana which led to the launch of a new activity, the Network for Analytical and Bioassay Services in Africa (NABSA) and IOCD contributed launching funds. There has been strong support from the University of Botswana and additional funding for NABSA has come from a variety of international sources including USAID, UNESCO, International Programme in the Chemical Sciences (Uppsala) and TWAS.

Coordinated by Berhanu Abegaz at the University of Botswana [168], NABSA's objectives are:

- To promote the development of scientific activities in Africa by offering analytical, bioassay and literature support services to chemists.
- To cooperate with active scientists in a joint short-term intensive-research undertaking by inviting them to the reasonably well equipped laboratory in Botswana.
- To promote the professional development of young scientists by arranging sub-regional symposia.

NABSA collaborating centers contribute a range of spectroscopic facilities including 200–600 MHz NMR (Botswana, Ethiopia, Kenya, Lesotho, South Africa and Zimbabwe) (Figure 1.11). In the period 1998–2009, NABSA provided over 11 000 NMR spectra and over 2000 mass spectra to African scientists. Recipient countries of NABSA services have included Cameroon, Democratic Republic of Congo, Egypt, Ethiopia, Ghana, Kenya, Nigeria, Sierra Leone, South Africa, Sudan, Tanzania and Zimbabwe. More than 30 short-term visits to the University of Gabarone were arranged for chemists from different African countries [163].

From 2005, NABSA's focus shifted to research cooperation with research groups in selected countries and institutions, particularly in Cameroon, Ethiopia, Nigeria,

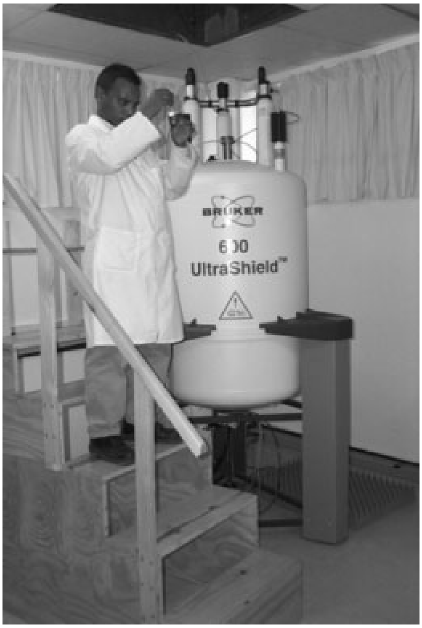


Figure 1.11 600 MHz NMR forming part of the NABSA analytical service at the University of Gabarone, Botswana. Photo from B.M. Abegaz.

South Africa, Tanzania and Zimbabwe, in order to help build and strengthen capacities and increase the overall impact of the collaboration. The NABSA centre itself has been involved in at least 63 publications in peer-reviewed international and regional journals Productive NABSA collaborations include a range of phytochemistry studies aimed at structure elucidation and the identification of bioactive natural products, such as anthraquinones [169]; Studies of Lathyrism, a disorder produced by toxic non-protein amino acids from the grass pea (*Lathyrus* species, *Leguminosae*) [170]; identification of dimeric sesquiterpenoid lactones from a south African plant (*Dicoma anomala*) possessing anti-plasmodial properties [171], leading to patenting; and identification of insect antifeedant bichalcones from *Rhus pyroides* and development of a general synthetic method for C–C linked bichalcones [172, 173].

NABSA has been an important source of energy and momentum for strengthening Africa's capacity for natural products research. In 2006 a new aspect was initiated with the establishment at the University of Botswana of the Centre for Scientific Research, Indigenous Knowledge and Innovation (CESRIKI), which has facilitated the Research Visitors' Programme of NABSA and also introduced a range of bioassay capabilities. In 2009, a consultative meeting in Gabarone led to an initiative for the establishment of a Pan-African Natural Products Library (p-ANPL) as a repository for compounds that have been isolated, identified and screened. The Board is drawn from several African countries.

Other networks operating in the African region include:

- SEANAC (Southern and Eastern African Network for Analytical Chemists). Established as a result of a SIDA-funded workshop in Gabarone in 2002, SEANAC's objectives are to (i) promote analytical chemistry in the region through collaboration, research, research training, teaching and information sharing; (ii) facilitate inventory, access, operation, maintenance and repairs of analytical equipment; and (iii) collaborate with organizations with similar aims [174].
- AAPAC (African Association of Pure and Applied Chemistry). AAPAC's objectives are to (i) provide a forum for the exchange among scientists and development agents of scientific information on the state of the chemical sciences in Africa; (ii) foster research in the chemical sciences; (iii) cooperate with other international bodies which pursue aims and objectives similar to those of AAPAC; (iv) promote mutually beneficial interdependent linkages between industry and other entrepreneurial bodies on the one hand and research institutes, including universities, on the other [175].

1.7.5
National Funding for Research

While funding from public and private international sources is very important, the availability of regular, national sources of public funding is essential if a critical mass of researchers is to be established and maintained [176].

In the 18th and 19th centuries, as the pace of technological progress increased before and during the industrial revolution, most scientific and technological research was carried out by individual inventors using their own funds [177]. Historically, the development of national channels for funding scientific research in Europe and North America is relatively recent and lagged considerably behind these first waves of technological progress. Apart from military research, they were driven by specific challenges such as public health problems and by broader concerns about international competitiveness. Some examples to illustrate this include:

- The Royal Society of England, founded in 1660 as a learned society, received a government grant in 1850 to assist scientists in their research and to buy equipment [178]. But it was in the early the 20th century that the challenge of tuberculosis led to the establishment in 1913 of the Medical Research Committee and the realization that Britain was falling behind its competitors led to the establishment in 1916 of the Department of Scientific and Industrial Research to fund applied research and technological innovation [179].
- Germany's Kaiser Wilhelm Gesellschaft zur Förderung von Wissenschaft und Forschung (KWG), now the Max-Planck-Gesellschaft, was created in 1911 [180]. The Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) traces its origins back to its forerunner, the Notgemeinschaft der Deutschen Wissenschaft, which was established in 1920 on the initiative of Fritz Haber [181].

- Following Belgium's early industrialization and development of chemical industries (Box 1.2), it established the Fonds National de la Recherche Scientifique (FNRS) in 1928 [182].
- The Centre National de la Recherche Scientifique (CNRS) was created in 1939 and is the largest governmental research organization in France and the largest fundamental science agency in Europe [183, 184].
- In the USA, the first National Institute of Health was established in 1930 for medical research, but the main science-funding agency, the National Science Foundation, was not created until 1950 [185].

1.7.6
Gender Issues

Across the world, there is a substantial under-representation of women in science. In 121 countries with available data, women represent on average 29% of researchers. In 37% of these countries, they represent less than one-third. Only about 15% of countries have achieved gender parity, and only a handful of others have more women researchers than men. The proportion of women researchers is low in Africa (33%) and particularly low in Asia (18%) (Figure 1.12) [55].

Equality for women in all fields of human activity, including in science, is first and foremost a fundamental human right. In addition, as noted by the World Economic Forum [186] "Countries that do not capitalize on the full potential of one half of their societies are misallocating their human resources and undermining their competitive potential".

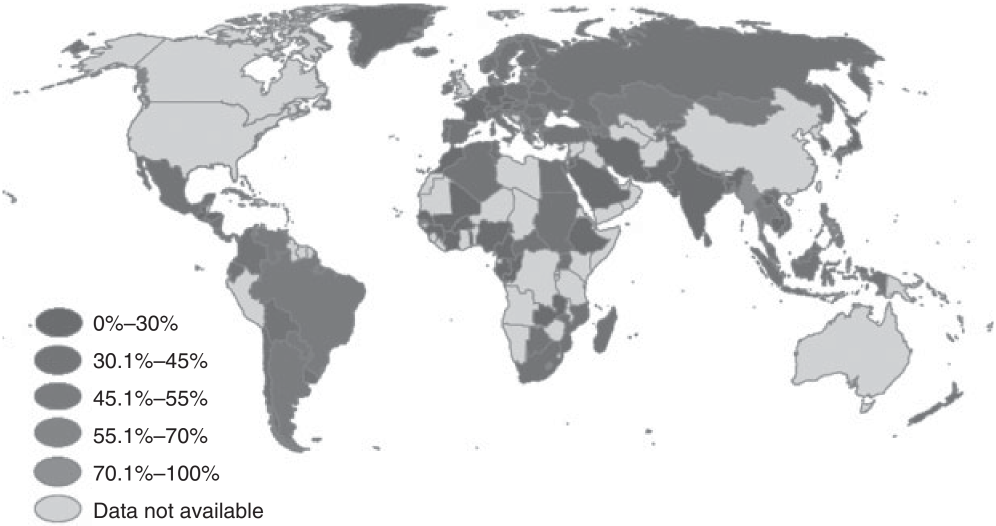


Figure 1.12 The gender gap in science. Women as a share of total researchers, 2007 or latest available year [55]. (Please find a color version of this figure in the color plates.)

To ensure that women achieve equality of opportunity in the field of science, countries need to institute a range of measures including ensuring equal access and treatment in school science programs and helping girls to build confidence in their science abilities; eliminating biases in university entrance procedures; and enacting anti-discrimination measures in employment [187].

1.7.7
Open Access

Access to published information is critical for scientists in order to enable them to assemble, understand and build on prior knowledge [188]. In chemistry and other sciences, there has been a rapid proliferation in the numbers and costs of journals over recent decades and libraries have found it difficult or impossible to keep pace. This problem has been especially acute for libraries in LMICs. As access to the internet has gradually extended to lower-income countries and some existing and newly established journals have introduced open access policies, there has been some improvement in access for those working in resource-poor settings. However, the situation is still far from satisfactory and there remains an unresolved tension between those who favor a policy of completely open, free-for-all access to scientific publications, those promoting special schemes which provide discounts and subsidies to scientists in certain LMIC-based institutions, and those wishing to preserve the commercial basis of publications. Learned societies in HICs are often finding this a challenging issue, since many produce leading journals in their subject areas and have become dependent on the income from journal subscriptions to maintain their financial viability [189–191].

Chemists need to work with their learned societies, professional bodies and funding agencies to seek innovative solutions that will maximize access to published material for those working in resource-poor settings.

1.7.8
Technology Transfer

The term “technology transfer” is used in two contexts, both of which are important to the subject of chemistry for development.

1) **Transfer between academia and industry:** In HICs, many universities have established “technology transfer offices” or “development offices” whose role is to assist academic researchers to find commercial applications for their discoveries. These offices may facilitate patenting, identifying commercial partners, start-up costs for small-medium size businesses, and so on. A number of technologically strong universities have established their own business parks as a further way of promoting commercialization.To date, relatively few LMIC academic institutions have adopted such models, so that their chemists and other scientists find it much more difficult to develop their ideas and may find it necessary to become involved in overseas partnerships instead.

LMIC governments and academic institutions can benefit from encouragement and assistance with establishing appropriate frameworks and building human resource capacities to be able to institute academic–industrial technology transfer arrangements as part of an overall enhancement of national innovation. There are instructive examples to be found in some successful initiatives in LMICs [192–194].

2) **Transfer of technology between countries:** The diffusion of technologies from one part of the world to another is not a new phenomenon. Prominent historic examples in the field of chemistry include a range of processes for chemical manufacture adopted from the Islamic world by European countries over a period of several centuries [195]. Interest now centers on the acquisition by LMICs of processes for manufacturing chemicals, pharmaceuticals and advanced materials. Tanzania provides an example (Box 1.8) of a country that has benefitted from giving greater attention to S&T and technology transfer [196, 197]).

Sources of technology for transfer may include the private sector [198, 199], international organizations [200] and public–private partnerships [201]. For LMICs,

Box 1.8 Science and technology (S&T) and the transfer of technology in Tanzania

S&T has made major contributions to Tanzania's economic development, including:

- Improvement of overall productivity by instituting structural changes in the models and methods of production which lead to greater efficiency and innovativeness in economic activities.
- Boosting exports by improving the quality of products, reducing the costs of production.
- Improvement of food security by supplying technical information to agri-producers and providing reliable markets for their products.
- Spreading income-earning opportunities by making technical information available to small entrepreneurs in rural and urban Tanzania.
- Upgrading the technical skills altitudes and productivity of the labor force through science and technology education and popularization.

Transfer of Technology

In the past, Tanzania had no deliberate strategies or plans for appropriate selection, acquisition and transfer of technology for effective integration of imported technologies with local capacity for R & D. However, currently, deliberate efforts have been put into place in order to make sure that the speed of technology transfer is effective and sustainable for example, establishment of the Tanzania Commission for Science and Technology in 1986 and the Centre for the Development and Transfer of Technology in 1994, to institute a workable mechanism for the coordination of capacity building in the selection assessment, negotiation, adoption, R&D, information exchange and extension services.

Policy/Regulatory Framework

The first National S&T policy was enacted in 1985 and revised in 1995, its major thrust being to establish a prioritized program for generating new knowledge and to determine strategies for

Continued

the application of S&T development in Tanzania. The broad objectives of the Tanzania S&T Policy are to:

- Promote science and technology as tools for economic development, the improvement of human, physical and social well being and for the protection of national sovereignty.
- Promote scientific and technological self-reliance in support of economic activities through the upgrading of R&D capabilities.
- Promote and encourage the public and private productive sectors in developing S&T.
- Promote active participation of women in S&T.
- Establish and/or strengthen national S&T institutions.

Legal Framework and Technology Policy Instruments

A scientific and technical advisory committee on S&T has been established in order to advise the President in addition to the Inter-Ministerial Technical Committee of the Cabinet.

A legal framework was laid down through the (Investment Promotion and Protection) Act of 1990, and the Tanzania Commission for Science and Technology Act No. 7 of 1986 which spells out the establishment of a National Centre for Development and Transfer of Technology. This Centre is charged with powers to establish rules and regulations for rationalizing the acquisition evaluation, choice coordination and development of technology.

In order to achieve the national goal of steady economic growth, maximum utilization of local resources and technology, expansion of technical education through development of local research units in enterprises, and long-term comprehensive technological policies integrated within the overall national development plans have been adopted by the Tanzania government.

Extracts from Tanzania *National Website [197]*

technology transfer may be the entry point for developing high value-added industries. In recent times, the growth of the chemical industries in Brazil, China and India have reflected a combination of technology transfer, adaptation and, in some cases, "reverse engineering" to devise new processes for making known high-value products.

The challenge for LMICs is to develop the combination of policy and economic conditions that favor inward investment, guarantee orderly labor relations and access to markets and that ensure the supply of well qualified scientists, managers and administrators.

1.8
Chemistry and Future Challenges to Health, Wealth and Wellbeing

1.8.1
"Glocal" – Thinking and Acting from Global to Local

Some have argued that the pursuit of S&T capability is not at all essential for lower income countries, but is an expensive luxury, while essential knowledge and technologies are best acquired by transfer from the richer nations that can afford to create them. But experience has shown that this view is not correct. Countries substantially accelerate their own development, enhance their competitiveness and strengthen their international negotiating positions by increasing their S&T capabilities. They need to be able to adapt and localize technologies even if these are created elsewhere; and they need the capacity to address their own problems, which are not always shared with higher-income countries (e.g., tropical diseases, local agricultural sustainability, specific water pollutants). Moreover, all countries need a basic capacity in fundamental areas like analytical chemistry in order to be able to monitor what is happening, identify problems and develop and apply solutions – for example, in relation to the quality of the environment or the quality and authenticity of pharmaceuticals in local supply.

These considerations are encouraging a growing realization that many problems have a dual character, involving a global dimension which requires joint international action on the one hand, but a local adaptation, application or focus on the other. Thus, as globalization progresses, the slogan “think globally, act locally” is evolving into a “glocal” or “glolocal” principle which requires everyone to “think and act globally and locally” and which has been adopted in the private sector [202, 203].

The following discussion of some major challenges provides a number of examples of the importance of this global–local duality of approach.

1.8.2
Agriculture, Food and Nutrition

The term “green revolution” describes a series of research, development, and technology transfer initiatives involving the development of high-yielding varieties of cereal grains, expansion of irrigation infrastructure, and distribution of hybridized seeds, synthetic fertilizers, and pesticides to farmers. They enabled many LMICs to increase their industrialized agriculture production and thereby to help meet the food and nutrition needs of growing populations (Box 1.9) [204]. Supported by the Rockefeller Foundation, the Nobel Laureate Norman Borlaug (who was also one of IOCD’s early advisers) played a leading role in the green revolution, developing new, high-yield dwarf wheat that resisted a variety of plant pests and diseases and yielded two to three times more grain than traditional varieties.

Overall, raised productivity in three of the world’s main staple food crops – rice, wheat, and corn – had substantial impact in a number of LMICs, including Mexico, Pakistan, India, and China. While this approach worked in Asia and other places where rice and wheat are the staple crops, it provided little benefit in Africa, where sorghum, millet, and cassava were consumed by the poor and where many countries also suffered from poor soil and uncertain rainfall, a shortage of trained agriculturalists and lack of technology. Borlaug was convinced that, while traditional plant breeding methods remained important, agricultural biotechnology and herbicide-resistant crops had a vital role to play in places like Africa [205, 206].

Box 1.9 The green revolution

"Record yields, harvests of unprecedented size and crops now in the ground demonstrate that throughout much of the developing world – and particularly in Asia – we are on the verge of an agricultural revolution.

- In May 1967 Pakistan harvested 600 000 acres to new high-yielding wheat seed. This spring (1968) the farmers of Pakistan will harvest the new wheats from an estimated 3.5 million acres. They will bring in a total wheat crop of 7.5 to 8 million tons – a new record. Pakistan has an excellent chance of achieving self-sufficiency in food grains in another year.
- In 1967 the new high-yielding wheats were harvested from 700 000 acres in India. This year they will be planted to 6 million acres. Another 10 million acres will be planted to high-yield varieties of rice, sorghum, and millet. India will harvest more than 95 million tons in food grains this year – again a record crop. She hopes to achieve self-sufficiency in food grains in another three or four years. She has the capability to do so.
- Turkey has demonstrated that she can raise yields by two and three times with the new wheats. Last year's Turkish wheat crop set a new record. In 1968 Turkey will plant the new seed to one-third of its coastal wheat growing area. Total production this year may be nearly one-third higher than in 1965.
- The Philippines have harvested a record rice crop with only 14% of their rice fields planted to new high-yielding seeds. This year more land will be planted to the new varieties. The Philippines are clearly about to achieve self-sufficiency in rice.

These and other developments in the field of agriculture contain the makings of a new revolution. It is not a violent Red Revolution like that of the Soviets, nor is it a White Revolution like that of the Shah of Iran. I call it the Green Revolution.

This new revolution can be as significant and as beneficial to mankind as the industrial revolution of a century and a half ago. To accelerate it, to spread it, and to make it permanent, we need to understand how it started and what forces are driving it forward. Good luck – good monsoons – helped bring in the recent record harvests. But hard work, good management, and sound agricultural policies in the developing countries and foreign aid were also very much involved."

Extract from speech by William Gaud, 6 March 1968 [204]

With the world's population expected to increase by 50% in the first half of the 21st century, there is now seen to be a need for another green revolution [49, 207] – one which provides adequate amounts of nutritious and affordable foodstuffs in high yield and through agricultural practices that do not require large increases in the global amount of land under cultivation and do not cause pollution of earth, water or air.

Chemistry has many roles to play in meeting these challenges, from soil chemistry to pollution monitoring, from creation of better methods of plant crop protection to helping develop new, more productive and more robust varieties.

1.8.3
Climate Change

There is now incontrovertible evidence that human activities during the last couple of centuries are responsible for a significant rise in average global temperature and a concomitant increase in extreme weather events such as floods and droughts and heat waves and severe winters. If continuing unchecked, this global warming and shifts in weather patterns threaten the lives and livelihoods of many millions of people, due to drought, desertification, floods, inundation of major tracts of land and even entire small island states, disruption of agriculture and the spread of water- and vector-borne diseases [208].

While there has been a temptation to see the impact of climate change as being something that will be felt some decades in the future, there is much evidence that the adverse consequences are already being seen, Three broad categories of health impacts are associated with climatic conditions (Figure 1.13) [209] and current excess mortality due to climate change may now be a few hundred thousand extra deaths per year [209, 210].

Furthermore, it is of special concern that the most severe impact of climate change is being felt by vulnerable populations who have contributed least to the problem. The risk of death or disability and economic loss due to the adverse impacts of climate change is increasing globally and is concentrated in poorer countries [48, 209].

Needed contributions from chemistry towards the international response to climate change involve a combination of measures to mitigate its extent and to adapt to the unavoidable consequences. LMICs will require substantial assistance, including technology transfer [211]. Chemistry has already made innumerable contributions to identifying climate-related problems (e.g., through environmental analysis of ozone depletion and greenhouse gas emission); understanding their underlying causes and contributing solutions (e.g., through studies of the roles of

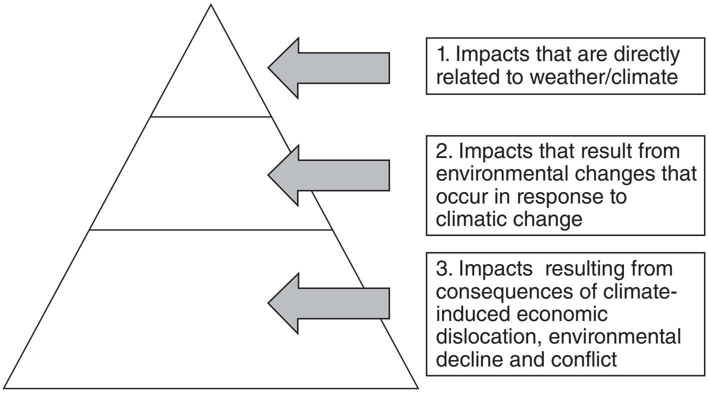


Figure 1.13 Health impacts associated with climatic conditions. Reproduced from [209].

gases like carbon dioxide and methane and the atmospheric photochemistry of fluorocarbon refrigerants and aerosol propellants).

Much more will be required of chemistry in the future, including better, cheaper and more robust field methods for environmental monitoring and impact assessment and developing new processes for energy generation, industrial production, materials recycling, and so on.

1.8.4
Energy

Intimately linked to the issue of climate change is the challenge of generating energy in an environmentally appropriate and sustainable manner.

World energy use (measured in kg of oil equivalent per capita) rose from 1338 kg per capita in 1971 to 1819 kg per capita in 2007, while world population rose from 3.8 billion to 6.6 billion during that period, representing an absolute increase in energy consumption of 236% [212]. With 80–90% of world energy production coming from the combustion of fossil fuels, there is an extremely urgent need to develop environmentally sustainable methods of energy generation, as well as methods for increasing the efficiency of energy use.

Among the many roles that chemistry is playing are:

1) devising ways of extracting and fixing carbon dioxide and other pollutants generated in burning coal and oil and reducing the emission of particulates that damage the respiratory system;
2) contributing to the improvement of efficiency of combustion engines, thereby reducing consumption;
3) developing new bio-fuels which reduce the net difference between current absorption and emission of greenhouse gases;
4) innovating new materials for the capture of sunlight and its transformation into energy;
5) creating new, environmentally clean processes for energy production, such as fuel cells.

1.8.5
Environment and Sustainable Development

Human activities such as the clearing of land for agriculture; diversion of water courses and extraction of water from underground water tables; extraction and transformation of raw materials to provide physical products and energy for power appliances; and the creation of domestic and industrial waste materials, all contribute to changes in the natural environment.

The pace of these changes has accelerated as the population of Earth has grown, especially in the last couple of centuries, but it is only within the last few decades that the extent of the problem has been recognized internationally [213] and a concerted global effort has begun to address the issues which have come to be expressed in the objective of "sustainable development". This term encapsulates the need to ensure that human beings can live in an environment free from pollutants and health hazards and that the sum of human activities does not cause degradation of the physical and biological environments of the planet. In particular, the Rio Declaration emerging from the UN Conference on Environment and Development, held in Rio de Janeiro in 1992, provided the fundamental principles and a program of action ("Agenda 21") for achieving sustainable development, establishing linkages among economic and social development and environmental protection [57]. This was followed up a decade later by the World Summit on Sustainable Development held in Johannesburg in 2002 [58].

Sustainable chemistry is understood as the contribution of chemistry to the implementation of the Rio Declaration and Agenda 21 and of follow-on processes such as the Johannesburg Declaration. The focus of sustainable development concerns in areas such as water, energy, nutrition, human habitation and the quality of the environment mean that chemistry has many central roles to play – in monitoring the environment, in understanding, preventing and mitigating adverse chemical/biological impacts of human activities, and in devising new, cleaner and more environmentally sustainable process. Strengthening capacity for analytical chemistry in LMICs is indispensable to achieving these objectives [214].

1.8.6
Health

The nature of health challenges faced in every part of the world is changing, as a result of shifting patterns of disease, the globalization of health threats, changes in the environment and in human behavior. Some of the key health challenges and roles for chemistry in meeting them are highlighted below.

Non-communicable diseases (NCDs – e.g., cancer, diabetes, heart disease, stroke) are becoming the most prevalent causes of ill-health and death everywhere – but in many LMICs they are appearing alongside still-prevalent *infectious diseases* – including some that are global challenges (e.g., HIV/AIDS and tuberculosis) and some specific to tropical regions (e.g., malaria, African and South American trypanosomiasis, visceral and cutaneous lieshmaniasis, schistosomiasis). Those diseases that are prevalent globally, like NCDs and HIV/AIDS, have attracted considerable R&D investment and drugs to prevent or treat them have become available, but often these are too expensive for use in LMICs and/or require functioning health systems able to support patients with chronic conditions – which many LMICs lack. Many of the tropical infectious diseases have been neglected by the global pharmaceutical industry and new or improved drugs are still needed [215]. Chemists have a central role to play in the discovery of new drugs for these communicable and chronic diseases – drugs that are safe, effective, affordable and suitable for use in resource-poor settings where there may be a dearth of cold chains, laboratory diagnostic and clinical analysis facilities and specialist medical facilities and personnel.

The *quality of pharmaceuticals in circulation* in developing countries has become an issue of very serious concern in recent years. Drugs that are sub-standard, illegal imitations and non-effective fakes are widely available in many LMICs, as well as authentic drugs that are out of date or have deteriorated due to poor conditions of transport and storage [216]. Every country needs mechanisms to identify such pharmaceuticals – requiring the establishment and maintenance of well-equipped and staffed national analytical laboratories able to conduct reliable and speedy analyses to internationally-recognized standards. Recently, there has been demand from some LMICs to be able to localize the production of pharmaceuticals essential to their health needs, which increases the need for local capacities for drug regulation and quality control.

Pandemics such as those caused by viruses responsible for severe respiratory diseases (e.g., SARS, avian flu, swine flu) have emerged as a serious global threat in recent years, with the potential to cause ill-health, death and economic disruption on a very large scale [217]. The importance of the contributions of clinical chemistry to diagnosis and of medicinal chemistry to developing preventions and treatments cannot be underestimated.

Demographic changes are occurring on an unprecedented scale of speed and scope. The world's population grew from a level of about 1 billion in 1800 to 2 billion around 1920 and then leapt to 6 billion in 2000. It is predicted to reach around 9 billion by 2050. The birth rate in HICs declined to around replacement level during the 20th century, so that most of the 50% increase anticipated in the 21st century will be in LMICs. While average population ages are rapidly increasing in HICs, creating serious challenges in the worker/dependent ratios, many LMICs currently have very high proportions of young people [218]. These demographic shifts have major implications for patterns of consumption and demands for physical and energy resources – and also for health. For example, the largest cohort of adolescents that the world has ever seen requires greatly increased attention to sexual and reproductive health services, including safe, effective and acceptable means of family planning, while the growing numbers of aging people will present growing challenges in the management of chronic diseases, including disabling conditions such as arthritis. Chemistry can make a major contribution, not only to the development of new drugs, diagnostics and medical devices appropriate to these changing populations but also to the creation of new materials that enhance their quality of life.

In 2007, for the first time the world's population living in urban settings was as large as the rural population and this *urbanization* trend is continuing. As most of the world's increase in population is happening in LMICs, a substantial proportion of the new citizens of the planet in the next half century will be living in cities in less wealthy countries, where currently many people live in very unhealthy conditions in crowded urban slums and informal settlements with poor access to clean water and sanitation [219]. Chemistry and allied sciences such as chemical engineering and materials, food, energy and sewage treatment sciences have much to offer in helping to ensure the availability of salubrious living conditions including healthy dwellings, clean water, sanitation and safe foodstuffs.

1.8.7
Intellectual Property

About US$ 1.1 trillion was invested globally in R&D in 2007, up from about US$ 525 billion in 1996. This intensification of investment in the creation of new knowledge has, in turn, fueled demand for rights over knowledge – that is, for the protection of intellectual property (IP). In 2007, 1.85 million patent applications, 3.3 million trademark applications and 621 000 industrial design applications were filed around the world. This creation of new knowledge is increasingly taking place in emerging economies and involving researchers in LMICs. As one indicator of the globalization of research, 21.9% of scientific articles in 2007 were internationally coauthored, three times as many as in 1985. Further scope for participation of LMIC scientists in the creation of IP is being provided by the increasing trend of "open innovation" – the tendency for firms to look outside themselves to satisfy their innovation needs, whether through traditional means, such as licensing, sub-contracting, R&D contracts or joint ventures, or through newer means, such as the use of problem-solvers on the Internet or open source cooperation [39].

Two aspects of IP issues are of particular relevance in the context of chemistry for development:

1) **Protection of IP rights of LMIC citizens and institutions:** This has been of particular concern in relation to the discovery or invention of useful processes and products by researchers in LMICs, and the protection of indigenous knowledge in areas like traditional agriculture and medicine.

With regard to this aspect, it is particularly important for LMIC governments to ensure that strong IP policies and legislation are developed and implemented and that governments and institutions in LMICs strengthen their capacities for the management of IP at the national levels and for the negotiation of IP issues at the global level.

- The World Intellectual Property Organization (WIPO) is a specialized UN agency established in 1967, dedicated to developing a balanced and accessible international IP system which rewards creativity, stimulates innovation and contributes to economic development while safeguarding the public interest [220]. WIPO's new Medium Term Strategic Plan [39] includes multiple technical assistance and capacity building activities.
- Among the tools available to assist in capacity building, the handbook of best practices in intellectual property management in health and agricultural innovation is an outstandingly useful resource [221].

2) **Protection of IP rights of LMICs to flexibilities under the rules of the World Trade Organization (WTO):** WTO deals globally with the rules of trade between nations, providing standards, enforcement and dispute settlement under the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) which came into effect on 1 January 1995 [222]. The TRIPS Agreement includes flexibilities in rules concerning the observance of patent rights

> on medicines and allows an exception that Members may exclude from patentability diagnostic, therapeutic and surgical methods for the treatment of humans or animals. In some cases, this can allow member states to import or synthesize drugs considered essential to their national health needs. However, the rules also make provision for agreements among parties which introduce additional restrictions. These "TRIPS Plus" variations have been extremely controversial in cases where they have the effect of reducing the ability of LMICs to protect the public interest. One notorious example has been the dispute over the rights of LMICs to access drugs for the treatment of HIV/AIDS without having to pay the extremely high prices that were being charged by multinational pharmaceutical companies [223–225].

Following the work of a Commission on Intellectual Property Right, Innovation and Public Health [226], an inter-governmental negotiating process under the aegis of the World Health Organization led to agreement on the WHO Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property [227]. In this document, Member States endorsed by consensus a strategy designed to promote new thinking in innovation and access to medicines, which would encourage needs-driven research rather than purely market-driven research to target diseases which disproportionately affect people in developing countries. The challenge now is to achieve consistency in the ways that member states approach IP issues in their dealings with WIPO, WTO and WHO.

1.8.8
Natural Resources Exploitation

Exploitation of the Earth's physical and biological resources has always been a feature of human activities and the pace and extent of this exploitation have increased markedly in the last two centuries – both driven by and feeding technology advances, economic growth and population expansion.

Many LMICs which have been mainly the source of raw materials such as minerals and primary agriculture products now wish to reap the economic and developmental benefits of increasing production and adding value to the materials through processing. At the same time, there is pressure on these countries to conserve their natural resources, engage in sustainable development and not follow the historic pathways set by HICs which have led to pollution, exhaustion of resources and loss of biodiversity.

Countries everywhere are now being faced with the challenges of dwindling stocks of many key natural resources such as minerals, oil, and gas, as well as a global reduction of biological diversity due to factors such as deforestation, overfishing, hunting, and excessive use of monocultures in agriculture.

Some examples of key contributions of chemistry to these challenges include developing cleaner, more efficient, less energy-intensive and less polluting extraction and refining methods for minerals; methods for the recycling of inorganic and organic materials, and new substitute materials.

Chemical studies of natural products have made exceptionally valuable contributions to human health and wealth. As an example of "chemical prospecting", Eisner [228] cites the example of ivermectin, a fungal metabolite of highly complex structure which has been marketed for treatment of parasitic worm infections in animals and human beings. As well as generating US$ 1 billion in sales, its donation by Merck to the World Health Organization laid the basis for the treatment and prospective eradication of river blindness (onchocerciasis) in Africa.

The exploitation of biological resources has become an area of particular concern. Conservation of biodiversity is considered vital for long-term human survival because plants, animals and bacteria can be the source of new nutrients, genes conferring resistance to crop pests, and drugs for combating diseases. This implies that studies are undertaken globally to uncover these valuable assets, but exploitation needs to conserve their stocks as well as ensuring appropriate rewards for their owners. Countries which have some of the most valuable and diverse and least studied biological resources – often LMICs – have sometimes experienced "biopiracy" in which samples of plants or knowledge about their uses have been taken abroad and exploited without benefit to the country of origin or to the local inhabitants whose indigenous knowledge has been the key.

Valuable lessons have been learned from the experience of LMICs that have developed ways to meet these challenges. One very instructive example has been that of Costa Rica, a tiny Central American country which covers 0.04% of the world's total land area, yet is believed to harbor about 4–5% of the estimated terrestrial biodiversity of the Earth. In 1989, Costa Rica founded a national institution to gather knowledge on the country's biological diversity, its conservation and its sustainable use. The Instituto Nacional de Biodiversdad (INBio) was established as a non-profit, public interest NGO with a high degree of autonomy and with initial financial assistance from the Swedish Cooperation Agency (SIDA) and the MacArthur Foundation [229]. In 1991, INBio instituted an innovative agreement with a multinational pharmaceutical company, in which Merck was granted the right to evaluate the commercial prospects of up to 10 000 plant, insect, and microbial samples collected in Costa Rica. In return for these "bioprospecting" rights, Merck paid INBio US$ 1 million over two years, and provided equipment for processing samples and scientific training. Merck also agreed to pay a royalty – to be shared equally by INBio and the Costa Rican Ministry of Environment and Energy – on the profits of any future pharmaceutical product or agricultural compound that was isolated or developed from an INBio sample. Subsequently, INBio negotiated several further bioprospecting contracts involving other partners than Merck, including Eli Lilly, with the result that income from INBio's bioprospecting activities rose to about US$ 1 million per year [230].

The Costa Rica example demonstrates the possibility of conducting research to identify new medicinal products from natural sources in an LMIC, in a way that preserves property rights, generates a financial return and encourages capacity building. The contrasting experience of Eli Lilly's efforts to work in Cameroon highlights the importance of clear government policies and laws that establish the legal basis for conducting bioprospecting [231, 232].

Many of the lessons were taken forward in the International Cooperative Biodiversity Groups Program, initiated in 1992 to make multi-disciplinary, multi-institutional awards to foster work on the three interdependent issues of drug discovery, biodiversity conservation, and sustainable economic growth [233, 234]. On a more modest scale, as a result of Eisner's encouragement, in 1996 IOCD established a program to facilitate and catalyze ethical bioprospecting. This has included work in South Africa, Kenya and Uganda – in the latter case, most recently assisting policy makers in the development of draft legislation [235].

1.8.9
Water

Unsafe water, coupled with a lack of basic sanitation, kills at least 1.6 million children under the age of five every year. The target under MDG Goal 7 aims to halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation. There has been some progress: between 1990 and 2006, over 1.5 billion people gained access to improved drinking water sources (usage of drinking water from improved sources rising to 87%, as compared to 77% in 1990) and over 1.1 billion gained access to improved sanitation (usage of improved sanitation facilities rising to 62%, as compared to 54% in 1990) (Figure 1.14). However, while the world is on track to meet the MDG drinking-water supply target by 2015 at the global level, many countries in sub-Saharan Africa and in Oceania are currently projected to miss MDG country targets, leaving significant portions of the population without access to improved drinking-water supplies. Moreover, the world is not on track to meet the MDG sanitation target by 2015. About 340 million Africans lack access to safe drinking water and almost 500 million lack access to adequate sanitation [236–239].

Meeting the challenge requires coordinated action by international agencies, governments and civil society partners, with a strong focus on sanitation [240] and major inputs from science and technology. Efforts among the various UN agencies with an interest in water and/or sanitation are coordinated by UN-Water [241].

The role of the chemical sciences is crucial, as highlighted in the report [242] of the Pan African Chemistry Network's "Sustainable Water Conference 2009". One of the key messages from this conference was that increasing Africa's capacity in analytical chemistry is imperative in order to support chemical monitoring and water management activities.

1.9
Conclusions

Chemistry has demonstrated its capacity to contribute substantially to increasing health, wellbeing and economic growth [243] and has great potential to assist in the development of LMICs. But what is needed for the future is not simply more of the same. The world has changed substantially in the last two centuries and

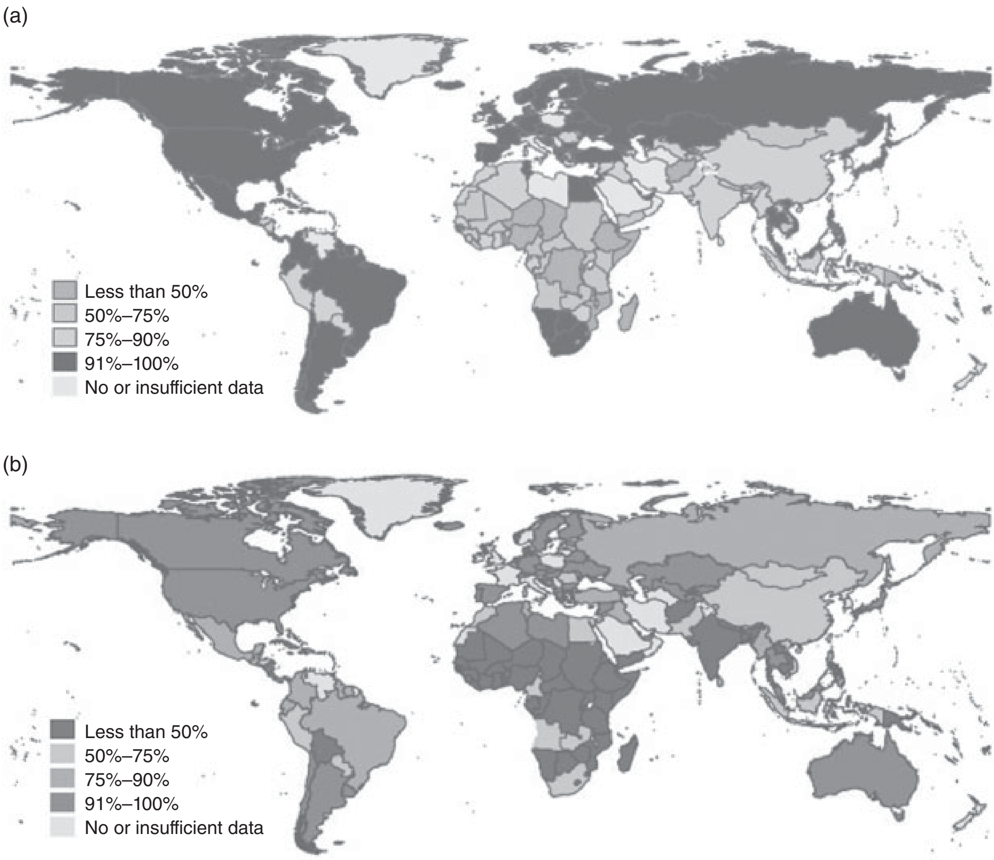


Figure 1.14 Global water and sanitation coverage [236]. (a) Improved drinking-water coverage, 2006. (b) Improved sanitation coverage, 2006. (Please find a color version of this figure in the color plates.)

many of the challenges it now faces are not only bigger but in some cases fundamentally different from those in the past. Globalization, urbanization, aging and population increases, threats of new diseases, pandemics, irreversible environmental damage and climate change, the revolutions in information technology, genomics and nanotechnology – all of these, individually and collectively, present new playing fields and new opportunities in an increasingly competitive and interconnected world.

Chemistry is a platform science. Its potential is, therefore, not only to help improve the human condition through its own direct contributions in fields such as the analysis and transformation of chemical entities, but also through the underpinning it provides to such diverse fields as medicine, genetics, biotechnology, materials and energy.

To take advantage of the new opportunities and to ensure that chemistry fulfils its potential, LMICs must invest in their own future by strengthening their science base and ensuring that the conditions exist for science, technology and innovation to flourish. This requires establishing sound policies, adequate funding mechanisms and environments where research is valued and its products utilized. It can be assisted by development partners, both public and private, who support the country's own policies and help build individual, institutional and country capacities to conduct, manage and exploit the fruits of science and technology [244].

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