Review

Bioprocesses: Modeling needs for process evaluation and sustainability assessment

Concepción Jiménez-González, John M. Woodley

1. Introduction

Process systems engineering offers many tools for the chemical engineer. Today, for example, modeling, simulation and process evaluation tools are routinely applied to optimization problems in...
the bulk chemicals and fuels sector, where small process improvements yield significant economic returns. In the last 20 years bioprocesses have become more common. In particular they have found application in the production of high value products such as pharmaceuticals (and their intermediates). The process engineering emphasis in these cases is on rapid process implementation (rather than optimized development). However, in recent years bioprocesses have also been applied to bigger volume products such as fine chemicals, bulk chemicals and fuels. In these cases process improvement is the emphasis since this will yield significant returns. In addition to the direct process improvements, bioprocesses have also frequently been justified on the basis that they are processes with potentially lower environmental impact than their chemical synthetic counterparts. The main synthetic operations in bioprocesses include fermentation, microbial catalysis and enzyme catalysis. Downstream options are dependent on the nature of the product (macromolecular or low molecular weight compounds (‘small molecules’)). Small molecules are frequently processed in a similar way to other chemical products, although dilute aqueous solutions bring specific problems which need to be addressed, both from the viewpoint of process optimization and the environmental footprint. For instance, the downstream processing of some small molecule bioprocesses could include large amounts of organic solvents for extraction from aqueous solutions. In these cases, the organic solvents require processing, recycle, control and ultimately safe disposal. Macromolecules require more specialist operations such as filtration or chromatography. However, in all cases the molecules are frequently sensitive to extremes of pH and temperature, placing specific restrictions and constraints on processing methods. Biocatalyst recovery (frequently for recycle) also necessitates filtration and centrifugation.

From this discussion it is clear that engineers and others involved in implementing new processes need to address a range of questions. For example: when should a bioprocess, rather than a chemical process, be implemented? If a bioprocess is to be implemented, can the existing infrastructure (feedstock, utilities and plant) be used? How can process plant be adapted for different biomass in different geographical regions? What is the optimum biorefinery? What options exist for process integration? What are the environmental, health and safety issues of bioprocesses in comparison with chemical processes? What is the environmental footprint of a bioprocess compared with its chemical counterpart? How can bioprocesses be designed to maximize process efficiency, minimize environmental impact, as well as maximize sustainability?

Many of these questions can currently be addressed qualitatively, but to have real value it is necessary to address these questions on a quantitative basis. In order to achieve this effectively therefore, computer-based tools are required. Over the last decades, process systems engineering has already developed many of the appropriate tools. Nevertheless, some further developments are required. For example, in the case of bioprocesses an extra option available to the engineer is the improvement of the catalyst itself. This requires models which take into account catalyst properties. In addition, one can see life cycle inventory and assessment (LCI/A) modeling tools and methods as a logical extension of process systems engineering. LCI/A methodologies allow for the estimation of environmental impact across the entire life cycle of a process or product. LCI/A estimations rely heavily on the characterization of the process and its unit operations using process systems engineering modeling and simulation techniques.

Hence we are now at the point where process engineering tools need to be applied to the complete set of bioprocesses, including pharmaceuticals, fine chemicals, bulk chemicals and fuels. In this paper the specific role of process systems engineering and life cycle inventory and assessment in the development, design and improvement of sustainable bioprocesses will be discussed.

2. Scope

Biotechnology is an enormous sector of industry from high value, low volume products (such as pharmaceuticals) to low value, high volume products (such as biofuels). To date the majority of implemented bioprocesses have focused on the former group. The emphasis here has been on implementing processes effectively to meet the tough regulatory demands placed on such products. Rapid process implementation, rather than optimization, has been the necessary focus of process engineering (e.g. Pollard & Woodley, 2007; Woodley, 2008). The latter group of bio-based products (and associated processes), represent a different challenge. These are the new sectors of industrial (also called ‘white’) biotechnology where new opportunities exist for alternative feedstocks based on renewable resources such as biomass and clean processes with reduced solvent inventories, renewable catalysts and mild conditions for reaction and separation (e.g. Dale, 2003). Here there remain some significant hurdles to achieve full-scale implementation. For example, for cost-effective synthesis one can start from fermentation of starch or sugars (ultimately from biomass given suitably cost-effective pretreatment). However, fermentation by its very nature is a rather inefficient process with a significant amount of substrate/reactant required for cell energy, cell growth and other products. This inherent weakness for use in chemical synthesis has stimulated genetic and metabolic engineering methods to improve strains. A parallel development with protein engineering has developed around enzymatic catalysis. Furthermore, the new ‘bio-economy’ will require the development of a suitable infrastructure and, like the oil-based counterpart will demand very high yield processes meaning that process engineering for the future implementation and development of these processes will have an increasingly important role, alongside the biological methods for biocatalyst improvement. In addition, the timely identification of environmental, health and safety issues to be managed will be crucial to facilitate the development of sustainable bioprocesses. Most importantly it is imperative that any claims of ‘greenness’ are considered in the wider framework of sustainability. Attempting to assess and compare the sustainability of bioprocesses must have a holistic scope based on life cycle thinking, which is strongly based on the output of systems engineering modeling and simulation techniques. Given the maturity of the field of process systems engineering it is clear that many new opportunities will be forthcoming.

3. Industrial biotechnology processes

Three major types of bioprocess can be identified dependent on the nature of the biocatalyst. These are outlined beneath and the key process features are outlined in Table 1.

3.1. Fermentation processes

For a significant number of chemicals, the use of fermentation has become a standard alternative to fossil-based feedstocks and technology. Nevertheless the possibility of growing microbial cells on a variety of sugars (derived from renewable biomass) has re-invigorated interest in this area. The consequence is that fermentation at a large-scale will become more common in the future chemical industry. Many different types of fermentation process (using different strains to produce different products) can take place in the same process plant which is a significant advantage. The plant is relatively simple and the challenges lie in adequate mixing (sometimes with materials having complex rheology), suitable oxygen input (for aerobic processes) and process control. Downstream, the separation process depends on the product, but will nearly always need to avoid high temperatures and extremes of pH. The solvent is water, meaning that the dilute product stream combined
with the presence of many other products presents a significant process engineering challenge. Both large molecular weight and low molecular weight products can be made by fermentation. The processes either focus on low molecular weight products which can subsequently be used as platform chemicals or fuels or high molecular weight compounds such as enzymes (for application in a range of industries, including detergents, textiles and food ingredients) or therapeutic proteins.

3.2. Microbial catalysis

In fermentation, by definition, the catalyst is growing during the process. This means that some of the reactant (or substrate) will inevitably be diverted from the product towards the catalyst, lowering the yield. An alternative (for non-growth associated products) is to grow the cells first and subsequently carry out the reaction to increase the yield. This also enables the possibility of growth and reaction on different substrates (reactants) or under different conditions (such as temperature or pH) in each stage. Likewise the optimal cell concentration for conversion can be selected (Woodley, 2006) after growth and suitable media for effective product recovery have been chosen. For processes requiring oxygen it can be highly important to select the optimal cell concentration in order to avoid mass transfer limitations. Several tools are now available for evaluating the oxygen supply issues in such reactions (Baldwin, Law, & Woodley, 2006; Law, Baldwin, Chen, & Woodley, 2006). The three potential routes using microbial catalysis are shown in Fig. 1.

3.3. Enzyme processes

The presence of so many products at the end of fermentation or microbial catalysis is a consequence of the complexity of cells, where many enzymes catalyze reactions giving a spectrum of products as well as decreasing the yield of the desired product on the reactant. An alternative, for short pathways, is to isolate the enzymes and then immobilize them on a solid support or behind a membrane or via aggregation, such that they are large enough and have the right properties to be recycled (like a heterogeneous catalyst). In this way a yield of product on the catalyst of around 5–10 tonnes/kg immobilized biocatalyst can be achieved, which typically enables industrial implementation. Such an approach has been widely used to assist in the synthesis of high value compounds such as pharmaceuticals and a more limited number of well-known lower value products such as high fructose corn syrup (HFCS). Many of these processes have also been modeled (e.g., Chen, Baganz, & Woodley, 2007). Enzymatic processes can also be carried out using soluble enzymes (i.e., non-immobilized), although these present challenges in terms of separating and recycling the catalysts (enzymes) when compared with the immobilized enzyme processes.

4. The role of process systems engineering

4.1. Evaluation of process options

For some higher value products a bioprocess may be the only route to a given product (to ensure correct folding of a therapeutic protein for example or the synthesis of an optically pure pharmaceutical intermediate). However, the more usual situation is that there are other competing routes to the same product. Therefore, for now, biotechnology is just one of a number of options for the production of chemicals and fuels. The economic drivers for implementation depend on existing infrastructure, feedstock costs, feedstock availability as well as the efficiency of the relevant (bio)catalyst and (bio)process technology. At the same time, there are environmental drivers and, in the wider sense, sustainability drivers for the selection of different process alternatives.

One example of the current applications of process systems engineering is the estimation of global warming potential and the design of processes that minimize this impact. Glasser, Hildebrandt, Hausberger, Patel, and Glasser (2009) for instance have recently proposed using process systems engineering tools such as mass and energy balances, thermodynamics and process work balances to minimize energy use and greenhouse gas equivalents. This is an example of how process system engineering together with thermodynamics can be used to set metrics and targets against important aspects or impacts. It is also an example of current methodologies that tend to focus on one impact and its corresponding leading metric (in this case, energy consumption).

However, the sustainability drivers normally cover several impacts and are by no means simple, as they require the balance of different sets of goals and metrics that can present trade-offs in
some cases. Objective functions to be optimized should not exclusively be based on economics but increasingly also on sustainability metrics (e.g. Henderson, Jimenez-Gonzalez, Preston, Constable, & Woodley, 2008) and integrated with life cycle analysis. This will need to include evaluation of feedstocks and products as well as processes, including energy and mass integration. This presents a fascinating set of alternative routes and technologies from a given feedstock and/or to a given product(s). Process systems engineering has a particular role to enable such evaluations on a quantitative basis, not only from the process perspective, but also from the wider sustainability aspect. Quantitation is key since it enables rigorous comparisons and assessments, which build confidence in decision-making. Process systems engineering also brings the advantages of rapid computational methods. Such simulations allow alternatives to be quickly evaluated. This is important to enable the use of tools early in process and product development. Finally, the answer in a specific case to the problem formulated here will in addition depend on regional factors. Feedstock availability and cost is highly dependent on geographical location. A parallel set of evaluations concerning the need to retrofit existing plant, or build new plant, is also required.

4.2. Evaluation of platform chemicals

While the increasing cost of oil is driving particular interest in the production of new fuels from biomass there is little doubt that today of equal importance is the production of chemicals from biomass. Indeed for the supply of fuels in the future there are many potential sources aside from biomass. In a world with limited (or very expensive) oil it is less clear where the chemicals of the future will originate. There is currently an existing infrastructure based on the use of the seven established platform chemicals (toluene; benzene; xylene; 1,3-butadiene; propylene; ethene; methane). In the short term one could consider if we can use the same infrastructure and just create the seven chemicals from alternative sources. However, in the longer term it will be necessary to devise new processes based on a different set of platform chemicals. One group will be based around glucose (the hydrolytic product of starch and cellulose and therefore readily available from biomass). In a biorefinery it will be necessary to develop a structure which can manage a range of feedstocks, a range of technologies and a range of products. This presents a considerable challenge for design and optimization as well as process integration. An interesting example which illustrates the complexity and the challenge that lies ahead is the use of glucose or fructose to produce 5-hydroxymethylfurfural (HMF) or 2,5-furandicarboxylic acid (FDA) (Boisen et al., 2009). Greatest value is obtained by going the whole way from glucose to FDA. However even in this small reaction pathway there are many alternative technologies. Some can be integrated together, some give the required yield and selectivity, some are difficult to implement and others are untested at scale. This illustrates very well the challenge that design engineers face.

4.3. Process integration

The primary solvent for most bioprocesses, with a few exceptions, is water. Consequently the downstream process is frequently difficult and this is emphasized by the need to carry out separations at moderate temperatures. Given the dilute nature of the streams it is frequently the case that the majority of the costs and environmental, health and safety impacts are therefore in the downstream process. The dilute nature of the streams has historically also driven the need for energy-intensive separation. For example, in some fine chemical and pharmaceutical applications of biocatalysis, large amounts of organic solvents may be used in the extraction and purification of products from an aqueous biocat-
alytic reaction stream. For higher volume products, such as liquid fuels, removal of water becomes an essential requirement to reduce costs and avoid transporting significant amounts of water. In other cases the product may be integrated within a biorefinery concept although at some point water will need to be removed. Consequently the integration of water use, and reuse via recycle, is an essential part of the design of industrial bioprocess facilities. In addition, bioprocesses need to be designed with process synthesis and process integration approaches, thus avoiding a process that is efficient in one part and inefficient in another. Existing tools of mass and energy integration such as pinch technology will have an important role. The issue of water integration in a biorefinery is in many ways analogous to the issue of heat integration in a conventional refinery.

4.4. Biorefinery design

Two major types of biorefinery have been identified for the future, based on lignocellulose biomass utilization to provide a range of sugars (for subsequent (bio)catalysis or fermentation) and oil-based material (from biomass). In each case the current research emphasis on biorefineries is to ensure all the fractions of a particular biomass in a given situation are fully exploited. Likewise the development of downstream products is now being explored. For example glycerol (as a byproduct of biodiesel production) can be used as a platform chemical (for example via fermentation to produce 1,3-propanediol). Another interesting example concerns the production of bio-ethanol. This is widely developed as a fuel although there is considerable economic incentive for developing a range of other products (e.g. acetic acid) from ethanol. In other words using it as a platform chemical (Rass-Hansen, Falsig, Jørgensen, & Christensen, 2007). It is clear that evaluating integration of product and feed streams in this way, as well as the use of products as fuels or platform chemicals will be an important role for process systems engineering. From the sustainability viewpoint, the utilization of lignocellulosic material has perhaps the highest desirability, since these materials are typically of low value as a waste from other processes (e.g. bagasse). There is little doubt that the increasing range of technologies and opportunities as a result of enzyme-based or fermentation-based catalysis will give complex integration problems, which may require new tools.

4.5. Biocatalyst design

A particular feature of bioprocesses is the use of biocatalysts, which may exist in several forms as indicated earlier and where options exist for modification. At the simplest level as a protein (isolated enzyme), the options for swapping amino acids via protein engineering exist. New enzymes which have been modified may display new tolerance to reactor conditions such as temperature or pH and may also have improved selectivity or reactivity (activity) on a given (non-natural) substrate or reactant. Order-of-magnitude improvements have been found in a number of cases although understanding the most effective method of making changes to the enzyme depends on past precedent and, to some extent, structural knowledge (e.g. Hibbert et al., 2005). In the case of microbial catalysts, individual enzymes can be over-expressed (increasing reaction rate of a given cell) and the regulatory control scheme fixed to direct the carbon to give improved rates and yields (via metabolic engineering). Some start has also been made to the development of pathways where enzymes coming from a variety of sources are cloned into single host to make a new pathway via a combination of genetic engineering and de-novo pathway engineering (e.g. Chen et al., 2006). In all these areas it is clear that those involved in process systems engineering need to inform the biological engineers about what is required in a given case and set suitable targets. Philosophi-
cally it is interesting to note that process implementation may come via process improvements or alternatively via catalyst improvements. In many cases both will be required. Understanding the necessary balance between these areas, as well as their integration with each other will be important for the future development of the field. Process systems engineering is particularly powerful in its ability to predict and can therefore be used to direct decision-making and process development.

5. Assessing the sustainability of bioprocesses

As discussed before, bioprocesses have frequently been highlighted as greener chemistry or engineering, since they address many of the green chemistry and green engineering principles (Anastas & Warner, 2000) by offering reactions that are potentially more atom economic, operate under mild conditions, use mostly non-hazardous chemicals and have less protection/deprotection steps. However, this tends to be true mostly when looking at the reaction part of the process, in other words, the biocatalysis. However, it cannot be generalized when analyzing the entire process that in some cases may include the use of a large amount of organic solvents for downstream processing. This is one of the areas in which systems engineering, in conjunction with a transparent application of life cycle inventory and assessment methodologies can (and must) play a pivotal role.

Determining whether a process is sustainable (or ‘green’) is by no means a simple feat. It is more akin to a multi-variable optimization that is very familiar to systems engineers, and for which several proposals and methods have been presented (Carvalho, Gani, & Matos, 2006; Gani, Jørgensen, & Jensen, 2005; Grossmann & Daichendt, 1996; Uerdingen, Gani, Fisher, & Hungerbuhler, 2003). For an objective assessment of the sustainability of a process, there is the need to utilize the tools that systems engineers have developed during recent years and apply them with a life cycle approach. It is necessary to move from the basic analysis of the biocatalysis by itself (or reactions) and discreet unit operations (separations) and use a systems engineering approach. This implies utilizing multi-variate optimization techniques coupled with life cycle assessment methodologies for a more objective analysis of their ‘greenness’ or sustainability. This would allow us to develop bioprocesses that are sustainable by design, in such a way that they:

- optimize the use of material and energy resources,
- eliminate or minimize environment, health and safety hazards by design, and
- integrate life cycle thinking in the design.

In a more general sense, sustainable bioprocesses in particular, and processes in general are/will be the processes that:

- minimize environmental impacts,
- are economically viable, and
- are socially responsible (OECD, 2002).

Analyzing and comparing sustainability will require a comprehensive assessment that balances the three different spheres of sustainability (see Fig. 2). This can only be achieved through a multi-variate optimization that will account for environmental performance, economic viability and social responsibility (which includes health and safety aspects). In addition, these assessments need to leverage the tools of systems engineering to ensure the integration of a holistic approach that considers the entire life cycle of the process.

Another important concept when assessing the efficiency and the sustainability of processes is the differences between new process performance and retrofit performance. For instance, in comparing the sustainability or performance of a well-known process with a new bioprocess, a situation that one often encounters is the fact that initially, the new process may not have the same level of performance as the established technology, mainly because they are at different points in the development curve, and therefore the new process is sub-optimal. On the other hand, the established process can be retrofitted to increase its performance. Retrofitting and new process development is not a new concept from the systems engineering viewpoint. However, additional modeling work is needed to estimate the achievable performance limits of a fully developed process and an established process that undergoes retrofit. This will allow more meaningful comparisons without unnecessarily penalizing the new process for its lack of development, or the established process for the lack of timely retrofitting.

In the recent past there have been many attempts to measure the ‘greenness’ of synthetic routes, and the approaches have generated a series of ‘green metrics’. Most of the approaches have searched for a simple metric in an attempt to provide a low resolution view of how ‘green’ is a given process. E-factor was one of the first measures of greenness proposed to highlight the amount of waste generated in order to produce 1 kg of product (Sheldon, 1992, 2007). This metric, while simple to understand, has several key drawbacks by focusing on waste instead of efficiency, neglecting a view of the type of waste generated, not accounting for the relative impacts, and the lack of life cycle thinking. For instance, bioprocesses have in general large amounts of wastewater produced, which would indicate an extremely large E-factor, but at the same time the actual impact of the effluent might not be as large as an E-factor would suggest, since the waste is relatively benign. Additional metrics have focused on efficiency, especially on mass efficiency (or its inverse, mass intensity) which addresses the first part of the disadvantages of the E-factor (Constable, Curzons, & Cunningham, 2002; ACS GCI PR, 2008; Constable, Jimenez-Gonzalez, & Lapkin, 2008). However, it has been widely recognized that measuring the sustainability or even the
'greenness' of a process is a multi-objective optimization problem that must take into consideration the efficiency of the entire process regarding the use of mass and energy, the environment, health and safety characteristics of materials, and the inclusion of life cycle thinking amongst others (Constable et al., 2001).

Some efforts have been made to comprehensively address and compare the sustainability of processes in general and bioprocesses in particular. These methodologies have been employed in some instances to assess the sustainability, environmental, health and safety aspects of bioprocesses (Cowan, Oxenbøll, & Holm, 2008; Jimenez-Gonzalez, Constable, Curzons, & Cunningham, 2001; Jimenez-Gonzalez, Constable, Curzons, & Cunningham, 2002; Jodicke, Zenklusen, Weidenhaupt, & Hungerbuhler, 1999; Kim & Dale, 2005, 2006; Kim, Jimenez-Gonzalez, & Dale, 2009; OECD, 2002; Patel et al., 2006; Wolf, 2005). These methodologies attempt to measure the sustainability of bioprocesses and in some instances they compare bioprocesses with their chemical alternatives.

For instance, a technology comparison framework (Jimenez-Gonzalez et al., 2002) that accounts for environmental, health, safety and life cycle assessment impacts, was used to compare the established chemical process and a two-enzyme biocatalytic process for the production of 7-ACA (Henderson et al., 2008). The conclusion of this assessment was that the bioprocess was 'greener' when compared with the chemical process. This was driven by the fact that the chemical process uses more hazardous materials, requires about 25% more process energy than the enzymatic process and, has a larger life cycle environmental impact: for instance, uses approximately 60% more energy, 16% more mass (excluding water), has double the greenhouse gas impact and about 30% higher photochemical ozone creation potential and acidification potential impacts. However, although this type of assessment is useful and more common as time passes, there is an ongoing need for modeling methodologies that will seamlessly integrate sustainability factors during bioprocess design and development. Normally economic factors are an integral consideration, and since the 1970s environmental factors at the unit operation and sometimes process levels have been considered. Nevertheless the need for integrating and embedding sustainability principles into bioprocess design still remains an area of opportunity for process engineers. Systems thinking and systems engineering are the skill and the discipline that will need to play an important role to make this happen, and a holistic view of bioprocesses and their interrelations will be imperative.

5.1. Life cycle inventory and assessment

One of the tools to analyze systems holistically is life cycle inventory and assessment (LCIA). LCIA is a methodology used to evaluate the environmental profile of an activity or process from the extraction of raw materials to its end-of-life. The resource consumption and emissions are inventoried and assessed from the perspective of extraction of raw materials, production, transportation, sales, distribution, use, and final fate (Fig. 3). Depending on the goal and scope of the assessment, the boundaries can be set differently: for instance a ‘cradle-to-gate’ assessment might be adequate when comparing two alternative processes to the same product; or a ‘gate-to-grave’ assessment may suffice when comparing two different end-of-life technologies. The results of these assessments can be reported as direct inventory data (for example life cycle energy, life cycle mass, life cycle emissions), measures of individual potential impacts (such as global warming or acidification), or as an aggregate score or index for high-level comparison (for example Eco-Indicator 99). LCIA methodologies and standards are described in detail in the literature (CML, 2002; Heijungs, 1992; Hendrickson, Lave, & Matthews, 2006; ISO, 1997, 2006; PRé Consultants, 2001; US EPA, 2003).

LCIA methodologies are in a way an extension of systems engineering and provide a directly applicable framework to assess the sustainability of processes. In addition to the traditional environmental life cycle assessment (which has increasingly included health and safety impacts), life cycle costing (LCC, or total cost assessment, TCA) and the more recent social life cycle assessment (SLCA) attempt to complete the holistic view of sustainability (Heinrich, 2006; Hochschorner & Finnveden, 2006; Hunkeler & Rebitzer, 2005; Jørgensen, Le Bocq, Nazarkina, & Hauschild, 2008; Jørgensen, Hauschild, Jørgensen, & Wangel, 2009; Klöpffer, 2003; Rebitzer & Seuring, 2003).

In the area of bioprocesses, the application of LCIA is still not a widespread practice. There are however, examples on how several practitioners have applied LCA metrics primarily using case studies to better understand the wider environmental implications of bioprocesses and to compare them with chemical routes. This type of assessment has provided some key insights, such as the role of separations, a more systematic and holistic method to evaluating waste impacts, and the nuances of renewability (Cowan et al., 2008; Kim & Dale, 2005, 2006; Patel et al., 2006; Vink, Rabago, Glassner, & Gruber, 2003; Wolf, 2005). For instance, a comparison of a process using metal catalysts and one using biocatalysts for the enantioselective reduction of ketoesters in pharmaceutical synthesis was performed using a streamlined LCIA methodology. The analysis identified unit operations and reaction conditions that had the largest significance on the impact of the synthesis. It was also concluded that whether the metal catalysts were better than biocatalysts depended mainly on the work-up from the use of organic solvents and energy-intensive steps (Jodicke et al., 1999).

One typical example of the application of LCIA is the relationship of bioprocesses and the utilization of renewable resources. While the use of renewable resources is indeed a goal from a sustainability viewpoint, there is more complexity in evaluating ‘renewability’. For example, there are the material resources and the energy required to produce renewable materials, which in turn may (or may not) be renewable. There might also be other environmental impacts such as the use of toxic compounds such as herbicides that might pose environmental trade-offs. Therefore it is necessary to assess renewability from a life cycle standpoint. For instance, desired materials that are extracted from plants may be separated using organic solvents, and then isolated from the extraction solvent through a series of purification steps (for example additional solvent extraction or distillation). Another example is the proportion of non-renewable feedstocks as part of a material
supply chain and the contribution of those feedstocks to the overall renewability of the materials used in a bioprocess. For instance, the production process of furfural based on biomass utilizes materials such as sulfuric acid, methanol or carbon monoxide which are often derived from fossil sources; in addition to the energy which is sourced from renewable and non-renewable energy carriers. A further factor to consider is the potential competing use of land and the impact derived from potential land-use change, which at this time is an area of ongoing debate (Fargione, Hill, Tilman, Polasky, & Hawthorne, 2008; Kløverpris, Wenzel, & Nielsen, 2008).

Developing life cycle inventories and assessing the LCIA impacts of bioprocesses is not a simple endeavor given the large amount of data needed from different sources. The more materials that are involved in the bioprocesses, the more life cycle inventory data will need to be collected, verified and analyzed. On the other hand, the life cycle inventory data for biomaterials is not always available. While there have been efforts to increase the body of knowledge of life cycle inventories and impacts of bioprocesses and materials either derived from biomass or needed in bioprocesses, considerable challenges remain. These challenges have influenced the development and use of streamlined life cycle assessment methodologies and ab initio modeling approaches to estimate the life cycle impacts of bioprocesses and bio-derived materials. This is precisely one of the opportunities for systems engineering to add value, as the development of reliable, consistent, transparent, accurate and easy-to-use modeling and streamlined techniques for LCIA will continue to be an important need to be able to routinely assess the sustainability of bioprocesses.

In the future, the development of true sustainability assessments, with an embedded LCIA approach will be necessary, aligned with the early modeling needs highlighted in this article. In order to routinely assess sustainability of bioprocesses and to embed sustainability principles into bioprocess design and development, the following modeling needs can be highlighted:

- Better deterministic models of unit operations that are part of bioprocesses, such as fermentation, biocatalysis. This would need to include fundamental design parameters to design more resource efficient bioprocesses.
- Development and enhancement of property prediction packages that would facilitate estimations of resources (e.g. energy requirement) and the utilization of optimization techniques.
- More extensive use of process integration techniques on bioprocesses, especially at the development phase.
- Better understanding of life cycle inventory and impacts of bioprocesses and bio-derived materials.
- Increased understanding of the uncertainties in modeling bioprocesses, both from the viewpoint of process design and sustainability assessment.
- Improved consistency and transparency of LCIA methodologies as applied to bioprocesses.
- Improved streamlined LCIA methodologies that are easy to use by academia and industry alike.
- More routine application of multi-objective optimization techniques for sustainability assessments of bioprocesses.
- Enhanced understanding of the interactions of the environmental, social and economic aspects of bioprocesses for a holistic view of sustainability.

Addressing these modeling and process understanding needs will make it possible to integrate sustainability principles into process design and development in a far more rigorous manner.

6. Mapping modeling needs of bioprocesses—an example

Henderson et al. (2008) compared the chemical process and a two-enzyme biocatalytic process for the production of 7-ACA. We have discussed briefly the results of the assessment in terms of the life cycle impacts of both synthetic routes. We will now use that example to map some of the modeling needs of bioprocesses discussed in this paper.

Fig. 4 depicts the different phases evaluated in the assessment, which include the extraction of the raw materials and the production processes with their corresponding energy and waste treatment requirements. As can be seen in Fig. 4, the production of the final API, formulation, distribution, use and end-of-life considerations are not included in the assessment.

In terms of models used for raw materials, the life cycle impacts of the materials was modeled using a combination of life cycle inventory data developed by ab initio methodologies based on chemical engineering methods and principal component analysis.
to fill the data gaps. For most common chemicals and solvents, most of the life cycle information was available. However, for the bioprocess, as mentioned above, the availability of life cycle inventory data of substrates, enzymes and feedstocks was limited and remains under development.

The information describing the production processes was in its entirety taken from process descriptions, internal reports, batch records and process data, and no models were used. This type of data was available since the bioprocess had been run at the commercial scale. However, if the same type of comparison was intended to be repeated with a process in either a conceptual design stage or a process with limited development, it would not be possible given the lack of models.

Relatively standard models were available and used to estimate the lifecycle impacts of energy production and waste treatment. The waste amounts and compositions were estimated based on the process descriptions using mass balances directly. Energy requirements were also estimated based on process descriptions using typical heat transfer models. To calculate energy requirements, pure component physical property data gaps (e.g. heats of formation) were estimated using molecular modeling based on group contribution methods, specifically the Marrero and Gani method (Marrero & Gani, 2001). Nevertheless, there remains a need to increase the accuracy of the models to estimate pure component properties for complex molecules and enzymes.

7. Future outlook

The development of new bioprocesses as a complement to existing chemical and fuel production methods is an exciting endeavor that will occupy many process engineers in the future. There will be a particular role for process systems engineers in this developing sector with the advantages of quantitative decision-making tools and rapid simulation that this brings, including process design and sustainability principles. In the future suitable models will inform developments at the infrastructural level (evaluation of biorefineries, feedstocks and integration), the process level (evaluation of alternative technologies and process integration) as well as the catalyst level (evaluation of alternatives for protein and metabolic engineering). In addition, these models will allow the integration of sustainability principles into process design and development.

The further development of process systems engineering tools (including property prediction packages and the development of a database for bio-based molecules) will be required. To routinely assess sustainability of bioprocesses will require as well more robust and transparent environmental life cycle inventory databases of bio-derived materials; as well as better modeling and understanding of the social and economic aspects of sustainability and their relationships. Finally, an increasing dialogue amongst the biochemical engineers, biologists and other disciplines with related areas of expertise will be necessary to enable the vision of sustainable industrial biotechnology to be fully exploited.

Acknowledgements

The authors wish to thank GlaxoSmithKline’s Biotransformations Team in general, and Peter Sutton, Joseph Adams and Andrew Collin in particular for their contributions, input and support to this article and the development of bioprocesses.

References


