Education and training for industrial biotechnology and engineering biology

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Abstract: Industrial biotechnology is focused on the production of bio-based fuels, chemicals and materials such as plastics and textiles. Engineering biology, synonymous with synthetic biology, provides a platform technology that brings an engineering approach to harnessing biotechnology for industrial production. The two combine within the political construct of the future bioeconomy, in which bio-based gradually replaces fossil-based production. There are many barriers to this future, including technical, political and social aspects. Behind all of these is a need for a new form of workforce not seen before, in which various skills and knowledge bases merge and combine. The required multi- and interdisciplinary skills challenge higher education to get out of the discipline-dominated paradigm. This study examines some of the current and future critical issues and provides some examples of how higher education is rising to the challenge.

1 Introduction

Organisation for Economic Cooperation and Development (OECD) analysis suggests that innovation thrives in an environment characterised by a few key features, including a skilled workforce [1]. Skills will be central to enabling bio-production due to the newness of the subject, its multidisciplinary nature, the complexity of biology and bio-production, and the need for many stakeholders with different skills. Jobs for the workforce, not only research jobs, are a major goal of bio-production. This will only work well by rethinking education.

Industrial biotechnology includes the manufacture of biofuels, enzymes, and bio-based chemicals and materials. A key discipline of industrial biotechnology is microbiology. Life sciences PhD-level education remains focused on training for academic careers [2]. However, data from 2010 published in the National Science Board 2014 Science and Engineering Indicators show that a mere 29% of newly graduated life science PhDs will find a full-time faculty position in the United States (Fig. 1). Meanwhile in the Nature PhD survey of 2017, nearly 75% of (general PhD student) respondents said that they would like a job in academia as an option upon graduation [3]. The number of US post-doctoral researchers far exceeds the growth in the number of tenure-track job openings [4]. There are simply too many PhD students and too few senior posts [5].

The problems are far from new. As far back as 1995, a report expressed the need for change in the education of scientists and engineers [6]. This report was concerned that the United States was producing too many PhDs. It said that industry often complained that graduates were too specialised to accomplish the range of tasks they would be confronted with. Also, when scientists form small biotechnology companies, they are often placed in a managerial role in which they may have no training or know-how [7]. This has all brought about a call for a new type of PhD, one that offers much more breadth and flexibility.

2 Challenge of multi- and interdisciplinary education

Traditional scientific education and training has remained divided by disciplines such as microbiology, chemistry and computing. The long-standing conundrum of multidisciplinary education is the need for both breadth and depth. The challenge to higher education remains on many levels. For example, a central theme in bioeconomy strategies is sustainability. Training in sustainability itself begs multi- and interdisciplinarity as some of the depth skills needed are systems thinking, strategic planning, and evaluating environmental, social and economic performance. This educational conundrum for sustainability [8] is the same for industrial biotechnology and engineering biology: how to make the interdisciplinary approach not only substantive but also practical for early-career scientists.

3 Life sciences industry-wide issues

Some of the life sciences-wide industry issues are clearly crystallised in an American report [9]. Employer interviews identified several industry-wide gaps in the capabilities and talent of the workforce pool and proposed reasons:

- The life science industry has a decreased need for deeply trained senior scientists. There is an over-specialisation surplus, whereas employers are looking for a workforce with greater breadth and more soft skills.
4 Critical workforce gaps in bio-based manufacturing

Industrial biotechnology is the fastest growing subsector of biotechnology ahead of biologics and genetic modification (GM) crops [11]. However, this burgeoning industry is faced with skills gaps. Finding biologists is not the most difficult task for employers. Automation engineers specialising in high-throughput strain production critical to engineering biology-based manufacturing are rare. Managing automated systems will have to be a skill set for graduates in biology and chemistry in the future [12]. We see the reality of this hitting soon with the large sums being raised by companies like Zymergen and Ginkgo Bioworks, the latter now valued at an estimated $1.3 billion. For a long time, it has also been difficult to find fermentation staff: this is the province of the biochemical engineer, who combines the mathematics of cell growth with bioreactor and bioprocess design. Yet bio-manufacturing is the common operation that links together all the different market sectors of the world’s biotechnology industry.

Perhaps hardest to find of all are employees well versed in experimental design and statistics, especially now that large data sets are becoming more common [13]. Big data is creating an imperative for more complex design that enables fewer experiments and trials. Scientific irreproducibility – the inability to repeat others’ experiments and reach the same conclusion – is a growing concern. Yet few early-career researchers receive formal instruction on topics like experimental design and flaws in statistical analysis [14].

This diverse group of employees is essential for a functional engineering biology-based production plant, but remains rare as this business sector is a small niche. As sector growth is difficult to forecast, it challenges governments to predict how to invest in and reform higher education to create a workforce that matches the growth dynamics of the sector.

4.1 Bioinformatics may be a major roadblock

The bottleneck for the growing industrial biotechnology industry is shifting to bioinformatics and data mining. Data mining tools akin to the ones revolutionising social sciences and linguistics will become essential. The Short Read Archive at the US National Center for Biological Information is set to exceed a petabyte [15]. As high-throughput sequencing is increasingly deployed, the acquisition of genomic information is also rapidly increasing. DNA synthesis cost has dropped sharply during this century. These price decreases, combined with advances in next-generation sequencing, are increasing the need for and role of advanced software design tools. ‘Dry lab’ skills have traditionally been isolated from ‘wet lab’ ones. Nevertheless, bioinformatics requires deep knowledge of biology theory and mathematics/computing. These fields are usually not taught in depth in the same programme in higher education, and this is but one more challenge to be overcome.

5 Scientist as engineer and technologist

Engineering education depends on several key concepts that have been largely missing in biotechnology [16]: comprehensiveness of available relevant knowledge, orthogonality, hierarchy of abstraction, standardisation and separation of design from manufacture. Systems modelling and design are well established in engineering disciplines, but until recently have been rare in biology. The sheer complexity of biology has also hindered development of its formal mathematics. Synthetic biology has started to bridge the gap between biology and engineering [17]. However, this comes at a time of widely conflicting attitudes to engineering education. For example, only 4.4% of the undergraduate degrees awarded by United States colleges and universities are in engineering, despite an overall increase in the number of students. This compares with 13% of similar degrees awarded in key European countries and 23% in key Asian countries [18].

With the continuing relationship between technology and discovery, Botstein [19] contends that cell biologists in the next 50 years will have to be conversant with a broader range of concepts. This will range from physics through chemistry to genetics. However, they will especially need to know mathematical and computational methodologies that drive technology development.

The quantitative theoretical and computational component represents a fundamental departure from the tradition of the life sciences. Nevertheless, Tadmor and Tidor [20] stressed that modelling should not be construed as a replacement for experimentation. Indeed, large stores of practical and theoretical knowledge are essential for one to function in a laboratory environment. However, creating this depth of laboratory skills is among the most expensive and time-consuming elements of higher education.

This all leads back to the conflicting challenges of creating breadth, depth and adaptability. Professional engineering societies may be well placed to help tackle these challenges. Although their influences on education are usually indirect, they can help establish the norms and expectations that build ‘adaptive experts’ [21].

5.1 Chemical engineer as a role model?

Chemical engineers have played a tremendous role in generating and transferring the enormous benefits of the chemicals industry to society. The mathematics and thermodynamics of chemical engineering enabled the transfer of chemistry from the laboratory to full-scale industrial production, using crude oil as the raw material. For industrial biotechnology to fulfil its promise in a bioeconomy, these skills will be essential, with the new raw material being biomass. Chemical and biochemical engineers are key elements of the future bioeconomy because they alone can set the production agenda, knowing the process, energy, materials and cost elements [22].

6 Synthetic biology education: another key interdiscipline

The education system has been responding to the needs of the growing synthetic biology community. The number of courses in synthetic biology has grown rapidly, with at least 100 institutions involved [23]. However, many do not focus on industrial production. Therefore, industrial biotechnology courses, and organisations teaching them, are still very much pioneers.

7 Beyond science and engineering

Given the history of the GM debate, such matters as public perception will also shadow industrial biotechnology and engineering biology. There is already evidence that political and economic pressures will guide development of engineering biology [24]. Kuldell [25] argued that educational efforts that fail to equip students for these aspects of the emerging discipline are unsound. Public engagement, though fraught, is necessary for the acceptance of engineering biology and industrial biotechnology more broadly. Public engagement is weakened by a lack of a standard approach [26]. Policy makers could include social scientists and ethicists in strategies for developing and encouraging the uptake of bio-based products, and have this embedded in education. On the other hand, public engagement should not become a ‘mode of governance’ of research [27].

To make employees fit for the workplace, this education also needs to encompass other practices such as regulatory compliance, risk assessment and biosafety, and good manufacturing practice.
(GMP). These practices are not academic research disciplines. However, they can change rapidly, with far-reaching consequences for a small company. In-house training in GMP, for example, takes up considerable time and human resources. It can be a burden for small companies.

7.1 Many faces of regulation

Bio-based production creates regulatory challenges across boundaries as well. The use of wastes as feedstocks in biorefineries has regulatory mountains to climb [28]. The metabolically engineered microbes (i.e. process) are subject to genetically modified organism (GMO) regulation. At the same time, the chemicals and fuels (i.e. products), often being drop-in substitutes for fossil-derived materials, are subject to chemical regulations. These include the Toxic Substances Control Act in the United States and Registration, Evaluation, Authorisation and Restriction of Chemicals in Europe. More mundane, perhaps, but ever-present are regulations associated with health and safety, packaging and traceability.

8 Some approaches to industrial biotechnology and engineering biology education and training

The US National Science Foundation (NSF) Center for Biorenewables, a third-generation Engineering Research Center (ERC) established at Iowa State University in 2008, is currently a partnership between eight United States and four foreign institutions [29]. The ERC’s mission is based on research and education principles that seek to transform the existing petroleum-based chemical industry into an industry based on renewables [30]. It offers courses for school teachers, through undergraduate and graduate education.

8.1 Undergraduate courses: preparing the way

It is probably too early for entire undergraduate degrees to train biologists in industrial manufacturing. However, relevant science undergraduate degrees could be re-designed to serve as a platform for post-graduate study. For example, one of the key disciplines, microbiology, has curricula overwhelmingly dominated by medical microbiology. A re-orientation of microbiology undergraduate education could include quantitative skills that are important for success in industry. Students so equipped with skills in calculus, linear algebra, statistics, large dataset management and programming would be better prepared for future education in, and a career based on, engineering biology [2].

In Canada, two universities are strengthening undergraduate programmes in biotechnology. The faculties of science (biochemistry) and engineering (chemical engineering) at the University of Ottawa jointly offer an undergraduate biotechnology programme. The University of Guelph offers an undergraduate programme in biological engineering that focuses on fundamentals in bio-materials science, bio-systems analysis, bio-mechanics, instrumentation and digital control. The programme can be tailored to explore interests in the production of renewable fuels such as ethanol and biodiesel, sustainable bioplastics made from plant materials, the extraction and stabilisation of nutraceuticals, or the manufacturing of safe food products.

8.2 Taught and research masters

Industrial biotechnology lends itself well to a research master’s degree, emphasising practice-led research combined with relatively few taught modules compared with other graduate degrees. This sort of degree is designed in most cases to prepare students for doctoral research. However, it is also useful for those considering a career in the private sector where research is a key focus, but a PhD is not specifically required.

The University of Georgia Master of Biomanufacturing and Bioprocessing degree, a 2-year programme, claims a unique focus on the full bio-manufacturing experience with hands-on training and exposure to industrial grade equipment. Its curriculum includes academic courses in science (e.g. biofuels/biochemicals, pharmaceuticals manufacture) and business (e.g. finance, supply chain issues and manufacturing practices). Instead of producing a traditional thesis, students complete a research project resulting from a 400-h industry internship.

The University of Cagliari (Italy) Master in Chemical and Biotechnological Process Engineering combines the skills of chemical engineering with the needs of the biotechnology industry. A goal is to teach students how to use the increased knowledge of chemical, physical and biological sciences in order to develop advanced mathematical models for chemical and biotechnological processes.

8.3 Training PhD students in interdisciplinarity

The United States NSF had a flagship interdisciplinary training programme at North Carolina State University – the Integrative Graduate Education and Research Traineeship (IGERT), educating PhD scientists and engineers by building on the foundations of their disciplinary knowledge with interdisciplinary training. Since 1998, the IGERT programme has made 278 awards and has provided funding for ~6500 graduate students.

Research topics were selected specifically to transcend traditional disciplinary boundaries and so encourage teamwork. Diversity in the background of selected students was a factor in their preparation to solve large and complex research problems of significant scientific and societal importance – typical of the so-called grand challenges that engineering biology is supposed to be able to address. Insights from IGERT are provided by a personal communication from Professor Fred Gould (Box 1).

8.4 Massive Open Online Courses

The traditional on-campus experience could be radically changed by Massive Open Online Courses (MOOCs), which will enhance classroom and laboratory work. The evidence for the impact of MOOCs is still embryonic, although in the United States drop-out rates are remarkably high and accreditations are as yet negligible [31]. More analysis is needed as greater experience is acquired with their use. A number of MOOC platforms, such as Coursera [32] and edX [33], now offer a wide array of classes spanning engineering to molecular biology and all the building blocks in between that can provide the basic toolset to start practising engineering biology. A specialist MOOC for industrial biotechnology is offered jointly by the Technical University of Delft and the University of Campinas (Box 2).

MOOCs are easily scalable and adaptable, which are important benefits. Industrial biotechnology and engineering biology are expanding and changing rapidly. As a result, educational materials can quickly lose their freshness, if not their relevance. When the hard foundational work of creating a MOOC is done, software and screencasts could replace or upgrade course content in a matter of minutes. Inevitably hybrid approaches that have elements of the MOOC approach will emerge. For example, SynBio4All, being developed at the Centre de Recherches Interdisciplinaires in Paris, can be described as part MOOC, part open laboratory notebook, and part crowdsourcing discussion platform on synthetic biology [35].

8.5 Specialist training facilities

For early-career scientists, gaining access to bio-based production experience is difficult because universities do not normally have the relevant facilities. The National Institutes model in Ireland includes a dedicated facility for training in bioprocessing (the National Institute for Bioprocessing Research and Training, NIBRT). For a relatively small country, Ireland has a large pharmaceuticals sector. NIBRT provides a ‘one stop shop’ for bioprocessing training requirements [36]. The institute builds
One solution to a shortage of experienced managers in the industrial biotechnology industry and graduate programmes could use such a facility to expose students to industry working conditions.

We recently polled some of our now advanced molecular biology graduate students about their perspectives on the depth of their training. They were all confident that they could match their peers in genetics and entomology in terms of depth. They did say that they had taken a couple fewer disciplinary courses than their peers in those departments, but they had learned the important subject matter on their own. Some felt that it would take them one extra year to complete their degrees because of the interdisciplinary work.

Each of the cohorts did a group project that resulted in a publication or website. Students in our third (last) cohort have published two peer reviewed interdisciplinary articles as a group.

Source: Personal communication from Professor Fred Gould, North Carolina State University, December 2017

Box 2. edX course in industrial biotechnology

The edX course in industrial biotechnology is a joint initiative of TU Delft (the Netherlands), the international BE-Basic consortium and University of Campinas (Brazil). It provides the insights and tools for the design of sustainable biotechnology processes. Students use the basics of industrial biotechnology for design of fermentation processes to produce fuels, chemicals and foodstuffs [34]. Throughout this course, students are challenged to design a biotechnological process and evaluate its performance and sustainability.

Combining edX with other relevant courses can build the broader education that bioeconomy and industrial bio-based manufacturing seems to need. For example, TU Delft offers another MOOC course on responsible innovation. This discipline considers new technologies that are being developed in response to social challenges (e.g. food safety, smart cities, sustainable energy and digital security).

The TU Delft MOOCs are offered through the online edX platform, where MIT, Harvard and other universities have been making courses available to anyone with an internet connection since 2012. TU Delft chose to use edX partly because the platform allows publication of materials with an open licence, making it possible for others to use the materials.
An approach that creates a vocational workforce locally and separately from the universities – in technical and community colleges, for example – would take pressure off the universities. It would also create more jobs and investment in local, community and further education colleges. This aligns well with thinking that envisages creation of biorefineries and bioeconomy clusters in rural and semi-rural environments as a means of rural regeneration. One approach suggests an apprenticeship training route to keep day-release apprentices from companies close to the training centres. However, a ‘tyranny of small numbers’ has been identified in the UK, meaning that there is not a critical mass of apprentices in one geographical area to make it worthwhile for colleges to offer specialised industrial biotechnology courses [45]. This relates to industrial biotechnology and engineering biology being emerging sectors, and it will apply to any nation establishing bio-manufacturing.

The recently formed Industrial Biotechnology Innovation Centre in Scotland, jointly with three Scottish further education colleges, has established a Higher National Diploma in industrial biotechnology [46]. The qualification is intended to prepare students for employment as laboratory technicians, process operators and production scientists.

9 Limits of interdisciplinarity

We should also ask if there are limits to which interdisciplinarity can be taught for at least two reasons:

1. In the quest for breadth, depth may become too diluted. This could certainly be cause for concern in engineering degrees if professional bodies such as the Institution of Chemical Engineers [47] found too little depth to accredit engineers and courses fit-for-purpose.

2. The burden of learning required to become familiar, if not expert, in various different disciplines may be too great, which could be especially true within the time limitations of master programmes. The flexibility is greater within undergraduate degrees; nevertheless, careful attention would have to be given to curriculum design to prevent overload, with the attendant problem of student drop-out.

Regarding this latter point, it is worth remembering that the drop-out rates in STEM subjects (science, technology, engineering and mathematics) are already alarming: some 50% of American college students who major in STEM drop out [48].

10 Conclusions

Industrial biotechnology and engineering biology training requires a paradigm shift in how education is structured. Programmes are needed that encourage creativity and exploration, while harnessing the truly unique interdisciplinary nature of the field and harvesting the different forms of training highlighted above. To keep pace in a changing world, beyond the traditional debate of depth versus breadth in education, one of the answers lies in training for adaptability and dynamism. Pioneering universities answering this challenge are, and will be, training the next generation of creative venture builders. These graduates will be able to update and productively use their knowledge to drive innovation. The gradual shift to biomass from crude oil and natural gas as the raw material for production will present a plethora of technical difficulties. It will demand the ability to use knowledge co-operatively to create the factories and products of the future. In response, the shift calls for equally innovative education and bold reforms.

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