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An engineering makeover of biomedical research

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The clinical translation of research findings into improvements in human health can take decades. Engineers perform biomedical research with a solution-oriented mind-set, generating tools and concepts that enable the transformation of knowledge into medical solutions. In this light, bioengineering becomes the driving force for accelerating clinical translation and introducing new concepts in validation, prevention, diagnostics and precision therapy.

Technology-driven discovery

The optical microscope can be credited as the starting point of cell biology, enabling the cell to be identified as the building block of life for the first time. Similar to modern progress in genome sequencing or artificial intelligence, it serves as a powerful example of how technological breakthroughs can propel biological discovery. To address the challenges associated with collecting and analysing large-scale biological information, scientists have promoted multi-disciplinary research[1] to combine biological and technological skills (Fig. 1a). This synergy has drastically increased the rate of discovery – that is, building biological knowledge – but has not had a similar effect on the conversion of discoveries to solutions. Clinical translation remains slow and expensive, mainly focusing on drug discovery using trial-and-error clinical trials.

Bioengineering solutions

A century ago, physics was at the epicentre of scientific progress. Similar to biology, physics is a culture of discovery. However, the conversion of physics knowledge to solutions, for example, in mobility or communication, is not performed by the discoverer-physicist, but by problem-solving engineers (Fig. 1b). Although often misinterpreted to associate with engines and devices, engineering stems from the Latin word 'ingenium', a term associated with intelligence, design and creation, and denotes the culture of innovating and solving problems irrespective of the application field. In this regard, bioengineers may operate in the same knowledge framework as biologists, in analogy to electrical or mechanical engineers operating in the same knowledge field as physicists. Yet, engineers apply knowledge, and, where necessary fill knowledge gaps, with a design- and solution-oriented mind-set, to generate tools that can accelerate the pace at which products and solutions are reached.

Investing in bioengineering education

The distribution of current educational fields reveals that we have not yet reached a point at which we focus on problem-solving in the biomedical sciences. Visionary support from universities and the Whitaker Foundation has generated more than 90 accredited programs in bioengineering in the USA[2]. By contrast, Europe has been slow to invest in bioengineering departments and programs, with many countries not offering any or only a few dedicated bioengineering departments. An analysis of the total degrees awarded by different disciplines (datausa.io) reveals that even in the USA, natural sciences departments award roughly 190,000 degrees annually in engineering and 14,000 degrees in physics – a ratio of around 14 engineering titles to each physics title. By contrast, approximately 163,000 degrees are awarded in biology, but only 12,000 degrees in biomedical engineering or bioengineering – a ratio of 0.07. In Europe, this ratio is much lower. This educational imbalance between discoverers and problem-solvers may explain the strong focus on biomedical discovery, rather than translation.

From discovery to new medical concepts

Engineering could have a major role in the development of tools to improve, accelerate and reduce the costs in three key biomedical research functions – observation, analysis and validation of biomedical information. Importantly, bioengineering can go one step further to introduce new concepts in medicine and shift healthcare paradigms. This advance is enabled by precise problem definition and the design of tools and solutions that can redefine prevention, early detection and breakthrough therapies, as described below.

Biosensing and early detection

Moving away from symptoms-based medicine, continuous health-monitoring and early detection promise to improve treatment efficacy and reduce healthcare costs by initiating interventions at early time points in disease development. However, compared with drug discovery and development, the financing of research programs for early detection is substantially less. Intensifying advances of next-generation biosensor technologies, imaging methods and liquid biopsies could become a game changer in continuous health monitoring.

In particular, in vivo and in vitro biomedical sensors could bring the detection of diseases to homes in the framework of disseminated medicine. For example, portable and wearable sensors that go beyond measurements of heart beat or arterial oxygenation could detect disease-specific biochemical and pathophysiological markers[3–5]. Although more complex and expensive, imaging can also play a part in early detection – for example, the use of fluorescent agents to detect early small lesions in oesophageal endoscopy[6], which may save thousands of lives and €1–4 billion in healthcare costs (EU program ESCEND). Similarly, miniaturized ultrasound devices have enabled portable diagnostics[7].

Information and computation

Advances in observation technology, such as large-scale omics analyses, have led to the availability of huge biological datasets, generating new computational demands[8] and advancing deep learning and artificial

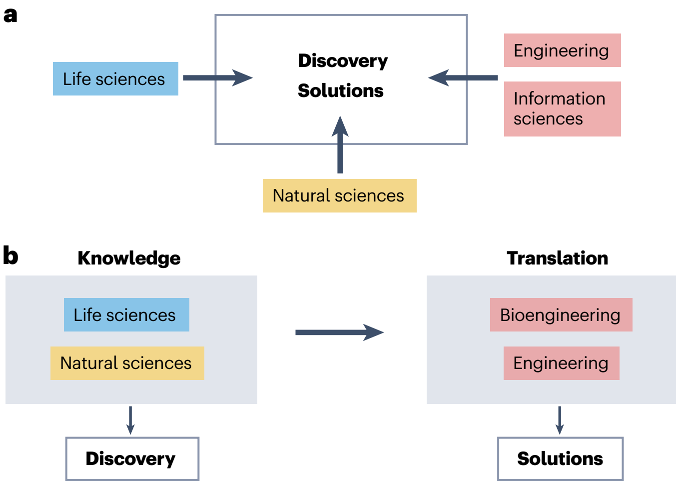

Fig. 1 | Engineering as the driving force toward clinical solutions. **a**, Multidisciplinary research denotes the synergy of different skills, typically resulting in accelerated discovery; however, multidisciplinary research does not necessarily lead to effective clinical solutions. **b**, Transformation of knowledge to solutions requires a different model than multidisciplinary research, in which attention is given to a problem-definition and problem-solving engineering culture.

intelligence methods and the development of digital twins — that is, models that can predict disease development and treatment efficacy. Nevertheless, computational solutions can only be achieved in the context of the information available in the analysed data, in particular, the relation of that information to the underlying problem; for example, the distinction between risk and disease characterization. Although several factors, such as genomic and lifestyle information, can be used to compute risk, continuous reporting on the actual disease status also needs to be considered, not just the statistical possibility of developing the disease. To achieve individualized disease characterization, omics information can be combined with frequent (continuous) phenotypic measurements provided by portable biosensors. This information can be compiled into a single health score that can better report on disease development over time, compared with risk assessment or binary classification of healthy versus diseased based on a threshold value of a diagnostic test.

Validation and cell engineering

Engineering solutions are also required to improve the efficiency by which new discoveries and hypotheses are validated for clinical use. Cell engineering and organ-on-a-chip technology could bridge the gap between cell culture or animal models and costly trial-and-error clinical trials. Complex cellular systems can be engineered based on human cells and biomechanical functionality to approximate ‘mini-organs’ that can resemble human conditions, including physical barriers and mechanical forces[9]. Although in its infancy, this platform constitutes a true engineering systems approach, in which a biological system is built to produce ‘outputs’ under controlled ‘inputs’. Although ethics need to be carefully considered, accelerated validation with robotic systems and advanced sensing and imaging techniques bear great potential to scale-up and potentially also minimize the number of animals used in research pipelines, contributing to the 3Rs rule of animal welfare.

Outlook

Bioengineering and biomedical engineering have existed for decades as a bona fide field in universities and postgraduate training programs. In these programs, students learn how to develop tools aimed at improving biological discovery and design devices for medicine. However, biomedical research is primarily conducted by discovery. We anticipate the growth of bioengineering as a discipline that accelerates the development of solutions for medicine and biology, in particular, by using technological advances to drive new concepts in validation, prevention, early diagnostics and precision therapy. Effective implementation of this translation catalysis requires action at all levels, including policymakers, funding agencies, educators, research administrators and scientists. Although biologists, physicians and engineers convert to problem solvers in biomedicine at a slow pace, there is an urgent need to actively promote bioengineering in the life sciences with educational and research programs that transform the notion of multidisciplinary research to engineering as the driving force towards clinical solutions, in analogy to the engineering growth seen in the natural sciences over the past centuries.

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Competing interests

V.N. is a founder and shareholder of the medical technology companies iThera Medical GmbH, sThesis GmbH, I3 Inc. and Spear UG.

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