Chapter 2

Biotechnology promises and expectations

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Chapter overview

This Chapter begins with a recognition of the diversity of biotechnologies and the different ways in which people use the term. We offer an inclusive description of the field of technologies in which we are interested. We then briefly survey the main fields of biotechnology in which significant advances are currently taking place. These are:

- cellular biotechnologies, including regenerative medicine;
- molecular biotechnologies, including transgenic plants and animals, and pharmaceutical biotechnology;
- genomic medicine, including personalised medicine, gene therapy and bioinformatics;
- synthetic biology; and
- nanotechnologies and nanomedicine.

We observe that the picture in each of these fields is of uneven progress with impressive technical advances often halted by scientific obstacles and contingent factors such as commercial investment and legal changes. We note the difference between this picture and the typical prospectus offered for new biotechnologies. We note an optimism bias with regard to prospective biotechnologies and that timescales for innovation are typically overestimated.

We identify a reason for the optimism bias in the patterning of expectations by reflection on the experience of past technologies. We examine the role of collective visions of technology futures, popular narratives about progress and the presentation of biotechnology in popular culture in fostering and reinforcing over-exaggerated expectations (of benefits or harms).

We note, however, that the experience of past technologies is often not an appropriate basis for inferences about the prospects of technologies of the future: the experiences are often poorly selected (more prospective technologies fail than succeed) and of questionable relevance to qualitatively different technologies with distinctive constraints.

These reflections recommend a methodological scepticism when assessing claims about prospective biotechnologies in order to make the foundation of decision making more robust. This scepticism can open up a space for reflection that averts two significant dangers of the dominant discourses on emerging biotechnologies, those of:

- linking biotechnologies to particular social objectives and thereby ignoring other benefits and reasons to promote the development of biotechnologies, and
- linking social objectives to particular biotechnologies and thereby failing adequately to consider and explore alternative means of meeting those objectives.

Introduction

2.1 In Chapter 1, we discussed the impact of biotechnologies of the relatively recent past and outlined some of the issues with which we will be concerned in this Report: the way in which technologies come to be researched, developed, implemented and diffused, and the part that deliberate choice, chance and necessity can play in these processes. We now turn our attention to fields of research from which biotechnologies of the future are currently emerging or may emerge. In this Chapter we will describe how some of those fields have developed and the promises and expectations that have been associated with them. We also consider how these expectations may be formed, modified and influenced by events and ideas. Our purpose will be twofold: firstly to provide some concrete examples of the kind of biotechnologies that we are concerned with in this Report, and secondly to advance our argument by drawing attention to the relationship between research and innovation in biotechnology on one hand and, on the other, the way in which biotechnologies are represented and discussed in different contexts. This will clarify how different *discourses on biotechnologies* influence biotechnology governance, and therefore on the emergence of biotechnologies themselves.

In what developments are we interested?

2.2 While the definition of 'technology' is commonly understood, the usage of substantive terms 'a technology' and 'a biotechnology' are subject to some variation and vagueness. Many of the distinctions that are made within the field of biotechnology serve pragmatic purposes (for

example, to assign research to a funding stream), rather than being intrinsic to the technologies themselves.[51] In responses to our public consultation[52] and in the broader literature on biotechnologies, the term 'biotechnology' is used to refer to:

- broad 'fields' of knowledge (synthetic biology is a 'biotechnology' in this sense);
- programmes of research defined by specific objectives (genetic modification (GM) of food crops is a 'biotechnology' in this sense);
- techniques or procedures, often associated with a distinct kind of apparatus or machinery (DNA sequencing is a 'biotechnology' in this sense);
- specific applications of techniques or procedures (in vitro fertilisation (IVF) is a 'biotechnology' in this sense); and
- products themselves (a nanoscale biosensor device is a 'biotechnology' in this sense).

2.3 We have characterised biotechnologies as conjunctions of knowledge, practices, products and applications. We have adopted this characterisation to reflect our interest, in this Report, in how these elements are brought together. However, what distinguishes biotechnologies from other technological forms is that these conjunctions involve some biological element, system or process. We recognise that the term 'biological' can also be problematic and, indeed, that many of the most vivid controversies arise at the margins of its application (for example, at the interface between chemistry and biology). For pragmatic reasons, we use the term inclusively: it is not our intention to rule anything out of consideration, but rather to orientate ourselves in the direction of the biological without claiming to know precisely where it begins and ends. In view of our intention to examine cross-cutting issues raised by emerging biotechnologies generally, our interests include technologies that involve:

- the utilisation of an adapted or unadapted biological system, process or component in industrial production (for example, the use of animals as bioreactors or bacteria for biofuel production), and/or
- the modification of a biological system or process through addition, insertion or integration with a biological or non-biological component (for example, gene therapy, regenerative medicine, tissue engineering, transgenic crops), and/or
- the creation of a new biological product or system using biological or non-biological components (for example, bacteria- or plant-produced plastics, 'BioSteel'®, in vitro produced meat).

2.4 The difficulty of defining the class of biotechnologies as a whole and of drawing clear distinctions between different biotechnologies is compounded by the interweaving genealogy of emerging biotechnologies. The communication, convergence, cross-fertilisation and differentiation of knowledge is, undoubtedly, one reason for the apparent fecundity of the field. Nor are biotechnologies, however defined, uniformly either emerging or established: in each field there is a body of relatively accepted knowledge and practice, having reasonably well-established applications, and a constantly moving leading edge (often implying reinterpretation of established knowledge and reconfiguring of existing practice). Thus the label 'biotechnology'

[51] The distinction between genetic engineering and synthetic biology may not be absolute. For example, the production of a precursor for an anti-malarial drug (artemisinic acid), often cited as an instance of synthetic biology, may also be regarded as genetic engineering involving many genes. See: Ro DK, Paradise EM, Ouellet M *et al.* (2006) Production of the antimalarial drug precursor artemisinic acid in engineered yeast *Nature* **440**: 940-3, for details on the production of synthetic artemisinic acid.

[52] The Working Party's public consultation ran from April to June 2011. A summary of the responses, which contains a list of biotechnologies that respondents referred to in their submissions, can be found online at: http://www.nuffieldbioethics.org/emerging-biotechnologies/emerging-biotechnologies-consultation.

encompasses a number of established innovations connecting knowledge, practices, products and applications, but also other conjunctions in the process of being assembled.

Cellular biotechnologies

Regenerative medicine

2.5 The identification and isolation of stem cells in the 1960s opened up a new field of research into regenerative medicine, raising the possibility of replacing damaged or defective tissues.[53] Stem cells are the precursor cells of the different tissues that comprise the body. The properties of stem cells – their capacity for indefinite self-renewal and the ability to differentiate into more specialised cell types – give them a great range of potential applications. Stem cell research was given a significant boost by convergence with the science and techniques of embryology: in particular, the possibility of establishing laboratory stem cell lines from embryos[54] that have a capacity for differentiation into a large number of other cell types (pluripotency) has led to highly promising lines of research. Arguably, this promise has been central, in the UK, to securing a favourable disposition of the law and public attitudes to extending human embryo research for therapeutic purposes.[55] The applications at which stem cell research is aimed include treatment of a range of diseases (such as sickle-cell disease, anaemias and thalassaemias) and injuries (reconnecting damaged nerves after spinal injury to restore sensation and motor control). Other applications include disease modelling[56] and the production of *in vitro* models for pharmaceutical testing, to assess toxicity more effectively than in animal models and in a way that minimises the need for human trials.[57]

2.6 The 'holy grail' of stem cell research has, for many years, been the production of bespoke tissues for transplant. The initial hope was that 'therapeutic cloning' techniques could produce cell lines with the same genetic immunological characteristics as the person to be treated. Being able to produce such tissues would overcome both the lack of availability of suitable transplant tissue from human donors and the need to use immunosuppressant drugs in order to avoid the transplanted tissue being rejected by the recipient. If this could be achieved effectively, it would mean a potentially unlimited capacity to generate replacement tissues and even solid organs to replace diseased or damaged ones. However, stem cell research has encountered setbacks with therapeutic efficacy, tumour formation[58] and cell expansion, as well as ethical controversy heightened by the instrumental use of human embryos in some approaches. Progress with the translation of stem cell research into therapeutic applications has also been set back by commercial difficulties among leading innovators.[59] These difficulties are likely to be compounded by a ruling of the European Court of Justice[60] that excludes human embryo-derived inventions from patentability on ethical grounds, which may have significant repercussions for commercial investment in future human embryonic stem cell research.[61]

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[53] See early works on identifying and isolating stem cells: Siminovitch L, McCulloch EA and Till JE (1963) The distribution of colony-forming cells among spleen colonies *Journal of Cellular and Comparative Physiology* **62**: 327-36; Altman J and Das GD (1967) Postnatal neurogenesis in the guinea-pig *Nature* **214**: 1098-101.

[54] Evans MJ and Kaufman MH (1981) Establishment in culture of pluripotential cells from mouse embryos *Nature* **292**: 154-6.

[55] For example, in the passage of the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 (SI 2001 No.188) and Human Fertilisation and Embryology Act 2008.

[56] Grskovic M, Javaherian A, Strulovici B and Daley GQ (2011) Induced pluripotent stem cells — opportunities for disease modelling and drug discovery *Nature Reviews Drug Discovery* **10**: 915-29.

[57] For example, Stem Cells for Safer Medicines is a UK public-private collaboration developing stem cell resources for use in the early, high throughput, toxicology screening of potential new medicines. See: http://www.sc4sm.org.

[58] Gutierrez-Aranda I, Ramos-Mejia V, Bueno C *et al.* (2010) Human induced pluripotent stem cells develop teratoma more efficiently and faster than human embryonic stem cells regardless the site of injection *Stem Cells* **28**: 1568-70.

[59] For example, the withdrawal of the leading human embryonic stem cell firm, Geron, from therapeutic trials, citing scarcity of funding; see: Pollack A (2011) Geron is shutting down its stem cell clinical trial *The New York Times* 14 November, available at: http://www.nytimes.com/2011/11/15/business/geron-is-shutting-down-its-stem-cell-clinical-trial.html?_r=0. We will return to the issue of commercialisation of biotechnologies in Chapter 9.

[60] *Brüstle v. Greenpeace eV* (Case C-34/10), 18 October 2011.

[61] We discuss the importance of patenting for emerging biotechnologies in Chapter 9.

Molecular biotechnologies

2.7 One of the most significant advances in the field of biotechnology was the development of recombinant DNA technology in the early 1970s.[62] For the first time, this allowed the deliberate transfer of functionally characterised genes from one organism to another, with the aim of reproducing in the second organism the desirable traits identified in the first.

Genetic modification and selection of crops traits

2.8 One of the first biotechnology fields to catch the public imagination and galvanise opinions was agricultural biotechnology.[63] Despite the commercial failure of the first attempts to market GM tomatoes in the early 1990s,[64] take up of the technology in the US has since proceeded rapidly.[65] In the UK, by contrast, brief initial success with a similar product (Zeneca's GM tomato paste) was halted abruptly by poor sales.[66] Indeed, concern about the impact of GM crops on human health, the environment and economic wellbeing, has played a significant part in defining the political terrain of biotechnology policy in the UK and continental Europe,[67] with levels of distrust and suspicion aggravated by apparently poorly framed attempts on the part of policy makers to engage with them.[68]

2.9 These controversies have been further compounded, particularly with initiatives to introduce GM crops in developing economies, by concerns about economic and social implications, such as concentration of industrial supply chains, ownership of intellectual property, and selection of products and technologies that prioritise private producer benefits at the expense of public benefits. Although the main firms involved use alternatives such as marker-assisted and genomics-assisted breeding alongside GM (as these different strategies are likely to have different levels of effectiveness depending on the traits of interest), the major bottleneck with all of these technologies remains in identifying the combinations of genes and other conditions responsible for the traits of interest.

Transgenic animals

2.10 The power of recombinant DNA technology is that it has potential uses across all biological systems containing DNA. The same recombinant DNA techniques that allowed modification of plant traits can equally be used to breed animals with altered traits. Transgenic animals (with genes from different species inserted) are used routinely in research to identify gene function. For example, a gene (GFP) that gives rise to a fluorescent protein in jellyfish can be linked to gene sites in mammals to identify the protein encoded by the gene of interest by fluorescence. Transgenic animals have also been developed for industrial purposes through a procedure

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62 The initial application to the US Patent Office describing the recombinant DNA technique was applied for by Stanford University and the University of California in 1974. See: Beardsley T (1984) Biotechnology: Cohen-Boyer patent finally confirmed *Nature* **311**: 3.

63 GM crops were the subject of two earlier Nuffield Council on Bioethics reports: Nuffield Council on Bioethics (1999) *Genetically modified crops: the ethical and social issues*, available at: http://www.nuffieldbioethics.org/gm-crops and Nuffield Council on Bioethics (2003) *The use of GM crops in developing countries: a follow-up discussion paper*, available at: http://www.nuffieldbioethics.org/gm-crops-developing-countries.

64 Calgene's 'FlavrSavr' tomato was modified to alter the ripening process. Zeneca, under licence, introduced a tomato paste based on the same modification into the UK market. Ultimately, both products failed commercially. See: Bruening G and Lyons JM (2000) *The case of the FLAVR SAVR tomato*, available at: http://ucanr.org/repository/CAO/landingpage.cfm?article=ca.v054n04p6&fulltext=yes. See also: House of Commons Science and Technology Committee (1999) *Scientific advisory system: genetically modified foods*, available at: http://www.publications.parliament.uk/pa/cm199899/cmselect/cmsctech/286/28602.htm, at paragraphs 11, 22 and 25.

65 Vàzquez-Salat N, Salter B, Smets G and Houdebine L-M (2012) The current state of GMO governance: are we ready for GM animals? *Biotechnology Advances* **30**: 1336–43.

66 House of Commons Science and Technology Committee (1999) *Scientific advisory system: genetically modified foods*, available at: http://www.publications.parliament.uk/pa/cm199899/cmselect/cmsctech/286/28602.htm, paragraph 21ff.

67 See: Gaskell G, Einsiedel E, Priest S *et al.* (2001) Troubled waters: the Atlantic divide on biotechnology policy, in *Biotechnology 1996-2000: the years of controversy*, Gaskell G, and Bauer MW (Editors) (London: Science Museum).

68 Horlick-Jones T, Walls J, Rowe, G, Pidgeon N, Poortinga W and O'Riordan T (2004) *A deliberative future? An independent evaluation of the GM Nation? Public debate about the possible commercialisation of transgenic crops in Britain, 2003.* (Norwich: University of East Anglia).

known as 'pharming'. This involves using modified animals as 'bioreactors' to produce substances beneficial to humans. These include insulin for the treatment of diabetes and vaccines, which may be extracted, for example, from the animals' milk. Another example is the development of a method of producing an anticoagulant drug (ATryn) that involves extracting it from the milk of a transgenic goat. This was approved for use by the US Food and Drug Administration (FDA) in February 2009, and was the FDA's first approval of a biological product produced by a transgenic animal.[69] Another example is 'BioSteel®', the proprietary name for a protein extracted from the milk of transgenic goats that had been modified with genes related to the production of spider silk.[70] This product was expected to have a huge number of potential applications from medical sutures to body armour, although there have been difficulties in 'scaling up' to commercial production levels and the firm (Nexia) that produced it turned its attention to other military applications before it ceased trading in 2006. Research in this area – for example using transgenic silkworms – nevertheless continues, with a new firm, Kraig Biocraft Laboratories, established to commercialise research at the universities of Wyoming and Notre Dame in the US.[71]

Xenotransplantation

2.11 Transgenic animals have also been developed for the purposes of xenotransplantation (cross-species transplantation), in particular GM pigs.[72] Non-human, decellularised structural tissues such as pig heart valves have been used in surgical procedures for several decades and there has also been considerable research into the xenotransplantation of whole organs, tissues and cells. Xenotransplantation research has been performed since the mid-20th Century, but suffered considerable setbacks during the 1970s and 1980s (such as short survival periods of organ recipients following baboon-to-human transplants and what was considered then as the "insurmountable" problem of rejection).[73] However, recent advances in some areas, in particular the wide availability of pigs genetically modified for the purposes of transplantation, have led to considerable progress in xenotransplantation research during the last decade.[74] Although routine clinical xenotransplantation has yet to become a reality,[75] some authors note that – at least for tissues and cells, if not organs – there is a possibility that clinical implementation may occur in the near future.[76]

Pharmaceutical biotechnology

2.12 The current strategic focus of publicly funded life sciences research in the UK is largely on medical applications of biotechnology.[77] Biological drugs – recombinant proteins, such as insulin,[78] and monoclonal antibodies, such as trastuzumab ('Herceptin'®), which may be used to treat breast cancer – have been developed and introduced with varying degrees of success.

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69 See: US Food and Drug Administration (2009) *FDA approves orphan drug ATryn to treat rare clotting disorder*, available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm109074.htm.

70 Lazaris A, Arcidiacono S, Huang Y *et al.* (2002) Spider silk fibers spun from soluble recombinant silk produced in mammalian cells *Science* **295**: 472-6.

71 See: University of Notre Dame (29 September) *Notre Dame and University of Wyoming scientists genetically engineer silkworms to produce artificial spider silk*, available at: http://newsinfo.nd.edu/news/16934-notre-dame-and-university-of-wyoming-scientists-genetically-engineer-silkworms-to-produce-artificial-spider-silk.

72 Klymiuk N, Aigner B, Brem G and Wolf E (2009) Genetic modification of pigs as organ donors for xenotransplantation *Molecular Reproduction and Development* **77**: 209-21.

73 Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.

74 Such pigs have been modified in a number of ways, such as to prevent porcine endogenous retroviruses activation or to reduce or eliminate the expression of particular pig antigens, which can help to limit incidences of hyperacute rejection when transplanting into primates. See: Ekser B, Ezzelarab M, Hara H *et al.* (2011) Clinical xenotransplantation: the next medical revolution? *The Lancet* **379**: 672-83.

75 Dalmasso AP (2012) On the intersections of basic and applied research in xenotransplantation *Xenotransplantation* **19**: 137-43.

76 Ibid.

77 Department for Business, Innovation and Skills (2011) *Strategy for UK life sciences*, available at: http://www.bis.gov.uk/assets/biscore/innovation/docs/s/11-1429-strategy-for-uk-life-sciences.

78 The first genetic engineering firm, Genentech, was founded in 1976 to "develop a new generation of therapeutics created from genetically engineered copies of naturally occurring molecules important in human health and disease"; the firm began producing recombinant insulin from modified *E.coli* bacteria in 1978. See, generally, the Genentech website, especially the 'History' section, at: http://www.gene.com/gene/about/corporate/history/index.html.

Biotechnology has also had an impact on drug discovery and drug development,[79] offering a 'rational design' approach to developing drugs for targets identified through genetic sequencing as an alternative to traditional drug discovery protocols that screen candidate substances for likely therapeutic efficacy. Nevertheless, use of biotechnology approaches to benefit patients, as opposed to producers, has been questioned by some[80] while, in any case, the rate of appearance of new biopharmaceuticals has proved significantly lower than had been hoped.[81]

2.13 Another field of research within biomedical science has focused on preventing the progression of disease by silencing the genes responsible for the replication of cancers and infectious agents. 'Antisense' research from the late 1970s involved introducing a strand of ribonucleic acid (RNA) with a molecular composition that would bind to genes identified as responsible for replication of disease and suppress their expression.[82] However, the research encountered significant obstacles to therapeutic use, including difficulty in delivering antisense RNA to target locations and avoiding digestion by the body's natural defensive mechanisms. From 1998, when it was first demonstrated in animals,[83] attention shifted to RNA interference (RNAi) involving double stranded short interfering RNAs (siRNAs), which occur naturally and are thought to be significantly more effective than single stranded antisense.[84] Pharmaceutical firms are working on RNAi-based therapies in areas including pain killers, slimming aids, and cancer[85] and scientists have discovered many new classes of RNAs that are thought to be involved in a range of common diseases, including leukaemia, lung cancer, hepatitis C, and diabetes.[86] Scientists have suggested that the RNA interference effect is just the tip of the iceberg of a complex interconnecting network of gene regulation, which is still incompletely understood.[87] However, despite an early rush for patents in this area, the promise of this technology for therapeutic use has not yet been realised. As the problem of delivering the siRNAs to target sites in the body has proved durably resistant to solution,[88] many firms have begun to withdraw investment from this area.[89]

Genomic medicine

2.14 Personalised medicine is a concept that reflects a confluence of different scientific, technological and social disciplines and approaches. A previous Nuffield Council on Bioethics report on personalised health care considered in depth the notion of 'personalisation' in the context of medicine and health care.[90] It noted how personalisation may have a number of different meanings, but among these is the tailoring of medicine to the biological characteristics

[79] See: Galambos L and Sturchio JL (1998) Pharmaceutical firms and the transition to biotechnology: a study in strategic innovation *Business History Review* **72**: 250-78.

[80] Hopkins, Nightingale, Kraft and Mahdi noted "biopharmaceuticals, like NCEs before them, are increasingly focused on securing economic benefits for developers rather than clinical benefits for patients in areas of unmet medical need." Hopkins MM, Martin PA, Nightingale P, Kraft A and Mahdi S (2007) The myth of the biotech revolution: an assessment of technological, clinical and organisational change *Research Policy* **36**: 566-89. This may, of course, be due to the commercial conditions of innovation, which we discuss in Chapter 9, rather than inherent limitations of the technology.

[81] Ibid.

[82] Zamecnik PC and Stephenson ML (1978) Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide *Proceedings of the National Academy of Sciences* **75**: 280-4.

[83] Fire A, Xu SQ, Montgomery MK *et al.* (1998) Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans *Nature* **391**: 806-11.

[84] Elbashir SM, Harborth J, Lendeckel W *et al.* (2001) Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells *Nature* **411**: 494-8.

[85] Economist editorial (2007) Really new advances *The Economist* 14 June, available at: http://www.economist.com/node/9333471.

[86] Mack GS (2007) MicroRNA gets down to business *Nature Biotechnology* **25**: 631-8.

[87] Amaral PP, Dinger ME, Mercer TR and Mattick JS (2008) The eukaryotic genome as an RNA machine *Science* **319**: 1787-9.

[88] Leng Q, Woodle MC, Lu PY and Mixson AJ (2009) Advances in systemic siRNA delivery *Drugs of the Future* **34**: 721.

[89] Ledford H (2010) Drug giants turn their backs on RNA interference *Nature* **468**: 487.

[90] Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: http://www.nuffieldbioethics.org/personalised-healthcare-0.

of particular patients or patient groups (pharmacogenetics, stratified medicine).[91] The basic enabling technology for personalised medicine is molecular diagnostics.

Personalised medicine

2.15 Much of the interest in this area relates to genomic medicine developed alongside and as a result of the Human Genome Project (HGP) and associated research (such as the HapMap,[92] ENCODE[93] and various genome-wide association studies). During the early years of the 21st Century there was considerable discussion of how the completion of the HGP would lead to a new era of medicine – one focused on prediction and prevention rather than cure.[94] This would grow out of more powerful diagnostic techniques (such as monogenic or multifactorial genetic tests) and the use of this information to inform lifestyle changes, tailored pharmaceuticals or gene therapy. Despite the enthusiasm surrounding the completion of the HGP, however, and in common with other biotechnologies, the innovation system for genomics in health care has proved a more complex matter than simple technical diffusion.[95]

Gene therapy

2.16 Another emerging area of biomedicine is gene therapy, which involves treating disease caused by faulty genes or gene function by the introduction of new therapeutic genes directly into the patient's cells by means of delivery mechanisms (vectors), such as modified viruses. Although not dependant on the performance of the HGP (there were gene therapy trials in 1990, the year the HGP began), the identification of genetic mutations responsible for disease made possible by the HGP has greatly facilitated scientific research in gene therapy.[96] This field, too, has suffered from setbacks in clinical trials and the impact of these on commercial interest in gene therapy research.[97] More recent trial results, for a range of conditions including Parkinson's disease,[98] have led to renewed optimism among researchers in the field.

Bioinformatics and converging technologies

2.17 Information and Communications Technology (ICT) has had, and will continue to have, a significant role in the development of personalised medicine:[99] the (relatively) recent – and rapid – improvement in the global capacity to store, transmit and compute large quantities of data has had a profound impact on all the sciences, including biology and especially genetics.[100] Some have argued that the demands of medicine-related ICT will soon surpass those of other data intensive fields and that the realisation of a genuinely personalised medicine will rely upon sophisticated computer models of living people.[101] For example, the 'IT Future of Medicine'

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[91] Pharmacogenetics was also the subject of a separate Council report. See: Nuffield Council on Bioethics (2003) *Pharmacogenetics: ethical issues*, available at: http://www.nuffieldbioethics.org/pharmacogenetics.

[92] The HapMap is "a haplotype map of the human genome…which will describe the common patterns of human DNA sequence variation". See: International Haplomap Project (2006) *About the International HapMap Project*, available at: http://hapmap.ncbi.nlm.nih.gov/abouthapmap.html.

[93] 'ENCODE' refers to the Encyclopedia of DNA Elements, a project which aims to identify all functional elements in the human genome sequence and develop technologies to generate high throughput data on those elements. See: National Human Genome Research Institute (2012) *ENCODE Overview*, available at: https://www.genome.gov/10005107.

[94] See, for example, Subramanian G, Adams MD, Venter JC and Broder S (2001) Implications of the human genome for understanding human biology and medicine *JAMA* **286**: 2296-307.

[95] As a recent report from the PHG Foundation observes: "the prevailing rhetoric amongst basic science funders, researchers and many policy-makers both in UK and worldwide is that genomic medicine represents a revolution in healthcare"; however: "knowledge and experience is slowly gained by clinical research leaders and the process of embedding new practice in high quality care pathways throughout the UK is gradual and difficult." See: Burton H, Cole T and Farndon P (2012) *Genomics in medicine: delivering genomics through clinical practice*, available at: http://www.phgfoundation.org/reports/12093, p16.

[96] Goncz KK, Prokopishyn NL, Chow BL, Davis BR and Gruenert DC (2002) Application of SFHR to gene therapy of monogenic disorders *Gene Therapy* **9**: 691-4.

[97] Nature editorial (2009) Gene therapy deserves a fresh chance *Nature* **461**: 1173.

[98] LeWitt PA, Rezai AR, Leehey MA *et al.* (2011) AAV2-*GAD* gene therapy for advanced Parkinson's disease: a double-blind, sham-surgery controlled, randomised trial *The Lancet Neurology* **10**: 309-19.

[99] See, generally, Nuffield Council on Bioethics (2010) *Medical profiling and online medicine: the ethics of 'personalised healthcare' in a consumer age*, available at: http://www.nuffieldbioethics.org/personalised-healthcare-0.

[100] Indeed, the HGP would not have been possible without such advances.

[101] See: Wiederhold BK (2012) ICT: this transformer isn't science fiction *Cyberpsychology, Behavior, and Social Networking* **15**: 189.

project (ITFoM) has the ambition to "create the entirely new ICT that is necessary to enable models of human biochemical pathways, cells, tissues, diseases and ultimately of the human as a whole" in order to "identify personalised prevention/therapy schedules and side effects of drugs".[102]

Synthetic biology

2.18 Synthetic biology applies the knowledge and tools developed in analytical biology to synthesise biological entities. It might be understood as an extension of genetic engineering, drawing on expertise in molecular biology, computer science, chemistry, and engineering. While some argue that the difference between synthetic biology and genetic engineering is largely one of labelling, others treat them as distinct fields of research.[103] An early inspiration, at least for some biologists using a synthetic approach, was a desire to understand natural biological systems,[104] although engineers working in synthetic biology focus primarily on producing novel applications. The definition of the field is subject to ongoing debate.[105] Its aims are usually taken to include exercising control at the level of design, characterisation and construction, to increase the predictability of designed biological systems.

Engineering biology

2.19 A range of different research activities fall under the broad heading of synthetic biology. Parts-based approaches aim to construct standardised biological parts (normally made of DNA). The ambition is to design them so that they are interchangeable and can be combined in a modular fashion to make new biological devices, making biology easier to engineer.[106] The most well-known type of biological part is a 'BioBrick'®, a standardised, interchangeable, composable DNA sequence of defined structure and function, developed with a view to building biological systems in living cells.[107]

2.20 Alternative approaches include attempts to simplify existing genomes to make a 'chassis' which, it is hoped, will form a basis for new synthetic organisms that will perform useful functions (such as producing biofuels).[108] In 2010, one research group reported the creation of an entirely synthetic version of the natural genome of a bacterium (*Mycoplasma mycoides*) that was put into a recipient cell, which then replicated successfully.[109] Other approaches attempt to reconstruct existing viral genomes from scratch, including the polio virus[110] and the φX174

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[102] Lehrach H, Subrak R, Boyle P *et al.* (2011) ITFoM – the IT future of medicine *Procedia Computer Science* **7**: 26-9.

[103] For example, the European Commission, the UK Royal Society, the UK Royal Academy of Engineering and the UK Biotechnology and Biological Sciences Research Council (BBSRC) have all produced material treating synthetic biology as a separate field. See, respectively: European Commission (2005) *Synthetic biology: applying engineering to biology*, available at: ftp://ftp.cordis.europa.eu/pub/nest/docs/syntheticbiology_b5_eur21796_en.pdf; Zhang YW, Marris C and Rose N (2011) *Transnational governance of synthetic biology: Scientific uncertainty, cross-borderness and the 'art' of governance*, available at: http://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/publications/2011/4294977685.pdf; The Royal Academy of Engineering (2009) *Synthetic biology: scope, applications, and implications* available at: http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf; and, Balmer A and Martin P (2008) *Synthetic biology: social and ethical challenges - an independent review commissioned by the Biotechnology and Biological Sciences Research Council*, available at: http://www.bbsrc.ac.uk/web/FILES/Reviews/0806_synthetic_biology.pdf.

[104] Elowitz MB and Leibler S (2000) A synthetic oscillatory network of transcriptional regulators *Nature* **403**: 335-8.

[105] See, for example, O'Malley MA, Powell A, Davies JF and Calvert J (2007) Knowledge-making distinctions in synthetic biology *BioEssays* **30**: 57-65.

[106] Brent R (2004) A partnership between biology and engineering *Nature Biotechnology* **22**: 1211-4.

[107] The BioBrick Public Agreement, an attempt to make biological parts free for others to use, was launched at SB5.0 in June 2011. See: BioBricks Foundation (2012) *The BioBrick™ Public Agreement (BPA)*, available at: http://biobricks.org/bpa.

[108] Glass JI, Assad-Garcia N, Alperovich N *et al.* (2006) Essential genes of a minimal bacterium *Proceedings of the National Academy of Sciences* **103**: 425-30. In May 2007 the J. Craig Venter Institute filed a patent for the smallest genome needed for a living organism. See also the relevant patent application for this approach: Glass JI, Smith HO, Hutchinson CA, Alperovich N Assad-Garcia N (2007) *Minimal bacterial genome* United States Patent Application No 11/546,364 (filed Oct 12, 2006).

[109] Gibson DG, Glass JI, Lartigue C *et al.* (2010) Creation of a bacterial cell controlled by a chemically synthesized genome *Science* **329**: 52-6. Commentators are divided over how revolutionary this step has been: Bedau M, Church G, Rasmussen S *et al.* (2010) Life after the synthetic cell *Nature* **465**: 422-24. See also footnote 215.

[110] Cello J, Paul AV and Wimmer E (2002) Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template *Science* **297**: 1016-8.

bacteriophage.[111] The purpose of this research is to generate knowledge that could, for example, lead to new synthetic vaccines in response to viruses that are themselves "diverse and variable", such as those that cause severe acute respiratory syndrome and hepatitis C.[112] On a wider scale, protocell research involves the attempt to recreate living cells from very simple components,[113] with the aim of creating new forms of life.[114]

Metabolic pathway engineering

2.21 A related area that has been researched since the since the 1990s is the manipulation of existing metabolic pathways to produce new products, the most well-known example of which is the construction of an artificial metabolic pathway in *E. coli* and yeast to produce a precursor (arteminisinic acid) for an anti-malarial drug.[115] It has been suggested that an approach such as this could be used to produce therapeutically useful compounds for the treatment of cancer and HIV[116], as well as polyketides,[117] a class of drugs with a variety of uses, such as the production of antibiotics[118] and insecticides.[119] This approach is also being used to produce biofuels, although firms are currently experiencing difficulties in scaling-up production to commercially viable levels.[120]

Alternative biologies

2.22 Whereas these approaches involve pushing the boundaries of natural systems in order to learn more about them, 'xenobiology' research attempts to make a biology that is altogether different from that which is found in nature.[121] An example of this approach is the attempt to use different kinds of nucleic acid – for example 'xeno-nucleic acid' – as opposed to the familiar RNA or DNA that occur in nature.[122]

2.23 In its current incarnation, synthetic biology is a young field[123] which means that most of the discussion around it is prospective and promissory, with only a few examples, such as the production of artemisinic acid, drawn on repeatedly to justify its promise. In practice, synthetic biologists continually confront the complex and context-dependent nature of biological systems.[124] However, in recent years the field has generated much enthusiasm and, increasingly, funding, because it is application-oriented and is seen by governments as a potential source of economic growth.[125]

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[111] Smith HO, Hutchison III CA, Pfannkoch C and Venter JC (2003) Generating a synthetic genome by whole genome assembly: φX174 bacteriophage from synthetic oligonucleotides *Proceedings of the National Academy of Sciences* **100**: 15440-5.
[112] Garfinkel MS, Endy D, Epstein GL and Friedman RM (2007) *Synthetic genomics: options for governance*, available at: http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-genomics-report/synthetic-genomics-report.pdf.
[113] Deamer D (2005) A giant step towards artificial life? *Trends in Biotechnology* **23**: 336-8.
[114] Bedau MA and Parke EC (Editors) (2009) *The ethics of protocells: moral and social implications of creating life in the laboratory* (Cambridge, Massachusetts: MIT Press).
[115] Ro DK, Paradise EM, Ouellet M *et al.* (2006) Production of the antimalarial drug precursor artemisinic acid in engineered yeast *Nature* **440**: 940-3.
[116] Voigt CA and Keasling JD (2005) Programming cellular function *Nature Chemical Biology* **1**: 304-7.
[117] Heinemann M and Panke S (2006) Synthetic biology — putting engineering into biology *Bioinformatics* **22**: 2790-9.
[118] See: Baltz RH (2006) Molecular engineering approaches to peptide, polyketide and other antibiotics *Nature Biotechnology* **24**: 1533-40.
[119] Martin CJ, Timoney MC, Sheridan RM *et al.* (2003) Heterologous expression in Saccharopolyspora erythraea of a pentaketide synthase derived from the spinosyn polyketide synthase *Organic & Biomolecular Chemistry* **1**: 4144-7.
[120] Bullis K (2011) Why Amyris is focusing on moisturizers, not fuel, for now *Technology Review* 9 May, available at: http://www.technologyreview.com/news/427890/why-amyris-is-focusing-on-moisturizers-not-fuel.
[121] Schmidt M (2010) Xenobiology: a new form of life as the ultimate biosafety tool *BioEssays* **32**: 322-31.
[122] Pinheiro VB, Taylor AI, Cozens C *et al.* (2012) Synthetic genetic polymers capable of heredity and evolution *Science* **336**: 341-4.
[123] The term can be traced back to 1912 to Leduc's book *La biologie synthétique,* but the first conference called 'Synthetic Biology' (Synthetic Biology 1.0) was not held until 2004 at MIT. See: Syntheticbiology.org (2004) *The first international meeting on synthetic biology*, available at: http://syntheticbiology.org/Synthetic_Biology_1.0.html.
[124] Kwok R (2010) Five hard truths for synthetic biology *Nature* **463**: 288-90.
[125] See, for example, the 4 January 2012 speech 'Our hi-tech future' by the Minister for Universities and Science: http://www.bis.gov.uk/news/speeches/david-willetts-policy-exchange-britain-best-place-science-2012.

Nanotechnology

2.24 Nanotechnology, like synthetic biology, is not a single technology; instead it refers to a wide range of techniques and methods for manipulating matter on length scales from a nanometre – i.e. the typical size of molecules – to hundreds of nanometres, with the aim of creating new materials and devices. Some of these methods represent the incremental evolution of well-established techniques of applied physics, chemistry and materials science. In other cases, the techniques are at a much earlier stage, with promises about their future power being based on simple proof-of-principle demonstrations.

Nanoscale techniques

2.25 The most immediate impact of nanotechnology on the life sciences has been the use of new tools for investigating the nanoscale. Techniques such as optical tweezers have, since their introduction in the 1980s, allowed the properties of individual biomolecules and assemblies of biomolecules to be studied in conditions close to those found in nature. This has permitted the quantitative analysis of the mode of operation of biological machines such as molecular motors and ribosomes, as part of the new field of single molecule biophysics.[126] Other nanoscale technologies – such as quantum dots – have offered useful, though not transformative, additions to the experimental arsenal of cell biologists.[127] One long-standing ambition of bionanotechnology, which is potentially transformative, is the ability to read the sequence of bases of a single DNA molecule, dramatically reducing the time and cost of whole genome sequencing.[128]

Nanodevices

2.26 Biological inspiration underlies the idea of using DNA synthesised to a prescribed sequence as a building material for quite complex nanoscale structures, exploiting the precise rules of base-pairing to design desired self-assembly characteristics.[129] In the last ten years a series of new concepts have been demonstrated, including that DNA can be used as the basis, not just of nanoscale structures, but also of functional devices such as motors and logic gates,[130] as well as for efficient storage of diverse forms of information.[131] This field is becoming increasingly attractive as a result of continuing exponential falls in the cost of DNA synthesis and the increasing sophistication of the devices being created in the growing number of laboratories working in this field. Hybrid constructions involving biological molecular machines integrated with artificial nanostructures have also yielded striking demonstrations (for example "nano-propellers" powered by the biological rotary motor F1-ATPase)[132] and suggested potentially beneficial applications such as artificial photosynthesis combining functioning biological sub-cellular systems in synthetic constructs.

Nanomedicine

2.27 In the area of nanomedicine, there are already applications of nanotechnology in clinical use,[133] although, as in all the fields we discuss, the choice of terminology is underdetermined, and is

[126] See, for example: University of Oxford Department of Physics (2009) *Oxford molecular motors*, available at: http://www.physics.ox.ac.uk/berry/research/Techniques/Tweezers.
[127] Barroso MM (2011) Quantum dots in cell biology *Journal of Histochemistry and Cytochemistry* **59**: 237-51.
[128] For recent developments in genetic sequencing, see Box 9.1.
[129] Seeman NC and Lukeman PS (2004) Nucleic acid nanostructures: bottom-up control of geometry on the nanoscale *Reports on Progress in Physics* **68**: 237.
[130] Seelig G, Soloveichik D, Zhang DY and Winfree E (2006) Enzyme-free nucleic acid logic circuits *Science* **314**: 1585-8.
[131] Church GM, Gao Y and Kosuri S (2012) Next-generation digital information storage in DNA *Science* **337**: 1628.
[132] Soong RK, Bachand GD, Neves HP *et al.* (2000) Powering an inorganic nanodevice with a biomolecular motor *Science* **290**: 1555-8.
[133] Nano-oncology is a particularly good example of this, with several nanomedical applications either current or emerging. See, for example, the 2005 FDA approval of the drug 'Abraxane'® (an albumin-bound form of paclitaxel) for "treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy." The drug has a mean particle size of approximately 130 nanometres. See: US Food and Drug Administration

thus open to manipulation and historical reappraisal. The distinction is blurred, for example, between some older products, which used quite sophisticated formulation science, and what are now described as nanomedicines.[134] The potential contribution of nanotechnology to biomedicine is most obvious in addressing the significant challenges of drug delivery that bedevilled – and in some cases, thwarted – the development of biopharmaceuticals. The hope is that these may liberate entirely new classes of therapeutic substances. A number of physical and chemical mechanisms have been proposed by which nanoscale delivery devices might preferentially deliver a drug to a target, such as a solid tumour, or carry it across an otherwise impenetrable obstacle, such as the blood-brain barrier.[135] This has potentially important applications in facilitating the use of new therapeutic agents, such as proteins and antibodies,[136] nucleic acids (in the context of gene therapy or siRNA)[137] and stem cells and tissue engineering.[138] However, some of the earliest and most straightforward achievements of nanomedicine are expected to be in reformulating existing drugs to improve their efficacy and reduce their side-effects (incidentally extending the profitable lifetime of a drug after the expiry of an original period of patent protection).[139]

Timescales of emergence: a cross-cutting theme

2.28 From this brief survey of some of the current landscape of emerging biotechnologies, at least one cross-cutting theme emerges: it is that innovation in emerging biotechnologies typically takes much longer and is subject to many more vicissitudes than had been anticipated. This is due, to a significant degree, to the complexity and dynamics of the material conditions that make up the innovation system: funders committing and withdrawing investment, changing regulatory requirements, even geopolitical developments affecting the relative desirability of different military applications. In many cases, development of the original 'target' applications is derailed and the technology develops along a different pathway, finding expression in alternative, often unanticipated, conjunctions. Thus: 'BioSteel'® development moves from goats to silkworms, while the firm originally committed to developing it took its goats into the development of an antidote for nerve gas;[140] stem cell research initially focused on therapeutic applications has yielded a more immediately promising offshoot in predicting toxicity of medicinal compounds;[141] the microorganisms developed for biofuel production have found more profitable employment in the production of higher value products, including cosmetics.[142] The

(2005) *Approval package for application number 21-660*, available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2005/21660_ABRAXANE_approv.PDF and, more generally, Portney NG and Ozkan M (2006) Nano-oncology: drug delivery, imaging, and sensing *Analytical and Bioanalytical Chemistry* **384**: 620-30.

134 See: Duncan R and Gaspar R (2011) Nanomedicine(s) under the microscope *Molecular Pharmaceutics* **8**: 2101-41.

135 Farokhzad OC and Langer R (2009) Impact of nanotechnology on drug delivery *ACS Nano* **3**: 16-20.

136 Proteins and protein fragments, such as antibodies, can intervene with great specificity with biological processes at the molecular level, but in their bare form they are rapidly eliminated. 'Cimzia'®, approved in 2008 by the FDA for Crohn's disease, and in 2009 by the European Medicines Agency (EMEA) for arthritis, is a fragment of an antibody coupled to a water-soluble polymer. See: FDA (2008) *FDA approves Cimzia to treat Crohn's disease*, available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm116882.htm and EMEA (2012) *Cimzia*, available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/001037/human_med_001294.jsp&mid=WC0b01ac058001d124.

137 These, similarly, are difficult to deliver to a specific target without them being detected and destroyed by the body. (For siRNA see above, paragraph 2.13).

138 It is becoming clear that the fate of stem cells as they differentiate is strongly influenced by the local nanoscale mechanical properties and biochemical environment. See: Discher DE, Mooney DJ and Zandstra PW (2009) Growth factors, matrices, and forces combine and control stem cells *Science* **324**: 1673-7.

139 For example, 'Abraxane'®, which was approved by the FDA in 2005 (see footnote 133) is a nanoparticle-based formulation of an older anticancer drug (paclitaxel) which avoids the need to use a toxic solvent. 'Caelyx'® and 'Doxil'® are alternative names for a nanoscale formulation of another old anticancer drug called doxorubicin which was used in the EU and US respectively. This form was approved by the FDA in 1995, and the drug is encapsulated in molecular containers made from self-assembled lipid molecules. See: FDA (2012) *Drugs @ FDA*, available at: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm.

140 See PR Newswire (2004) *Nexia's military biotech drug Protexia® shows promise as a rescue therapy for civilian CW casualties*, available at: http://www.prnewswire.com/news-releases/nexias-military-biotech-drug-protexiar-shows-promise-as-a-rescue-therapy-for-civilian-cw-casualties-75819222.html.

141 California Institute for Regenerative Medicine (2008) *Stem cells in predictive toxicology: CIRM workshop report, July 7-8*, available at: http://www.cirm.ca.gov/pub/pdf/CIRM_Predictive_Tox.pdf.

142 See footnote 120.

path of biotechnology innovation is seldom either short or straight. If the pathway is imagined prospectively, as it often is, as one leading from basic research and proof of concept to marketable application, it is certainly long enough for political, commercial, medical or military priorities to change several times.

Biotechnology visions

2.29 Biotechnology research has made significant – sometimes extraordinary – advances, although these have rarely been made in a linear fashion. The advance towards imagined applications has often been held up, diverted, sometimes thwarted, by a variety of factors including investment decisions (stem cells, gene therapy, RNAi), public attitudes (GM crops), and ethical and legal constraints (embryonic stem cells), as well as bottlenecks and unforeseen intractabilities of biological science (for example, antisense, gene therapy, xenotransplantation). These factors are clearly not independent of one another: for example, longer than anticipated timeframes, or public opposition, or the appearance of a promising alternative, may lead to withdrawal of investment (as we shall consider in Chapter 9). Nor can they often be anticipated (as we shall consider in Chapter 3), although scientific researchers are, by professional disposition, usually wary of making definite predictions or ambitious claims.

2.30 However, the professional caution and scepticism of researchers is only one influence operating in what we have described as the discursive context surrounding biotechnologies, in which the interests and values of politicians, publics, entrepreneurs, media and institutions all play a part. Even if researchers, therefore, are able to resist the often considerable pressures to overstate their cautious and sober assessments of the prospects of emerging biotechnologies, others may still place a different construction on them. It is therefore not the formation of these representations in any one discursive context that is *necessarily* the source of dissonance, but their translation from one discursive context, in which they may appear with appropriate caveats and qualifications, into another in which they take up a place in relation to a *different* set of values and priorities. In other words, what is reported in a scientific journal can look very different when it is reported in the popular media. As we argued in Chapter 1, these representations are not inconsequential, because they can come to dominate the discourse through which conditions (like funding, investment, public support) that shape the emergence of biotechnologies generally are set. In the remainder of this Chapter we therefore begin to look at the formation of expectations and the role these play in emerging biotechnology governance.

The formation of expectations

2.31 Emerging biotechnologies are promissory by nature. Belief in the beneficial prospects of a particular biotechnological initiative is necessary, but not sufficient, to bring that technology about; on the other hand, scepticism about those prospects may be sufficient, but not necessary, to cause it to fail.

2.32 The securing of beliefs about the likelihood of future states of affairs, however, is dependent not only (or not even) on rational calculation but also on how expectation is structured by language, values and experience, and indeed how those come together in influential 'folk narratives'. An example of this is the frequently repeated assertion that the effects of a technology (positive or negative) tend to be overestimated in the short term and underestimated in the long term.[143] Observations of this kind have become powerful in structuring expectations about future biotechnologies but also in informing decisions that can contribute to bringing them about. For example, the Gartner consultancy's 'hype cycle' methodology offers an example of a structuring of expectation explicitly intended to inform choices that, for example, industrial decision makers might make, which might thereby contribute to bringing about the intended outcome through

[143] This observation, usually attributed to US scientist, Roy Amara, was used approvingly in 2010 in relation to the development of personalised medicine as an outcome of the HGP by the Francis Collins, the director of the US National Institutes of Health who described it as "the first law of technology". Collins F (2010) Has the revolution arrived? *Nature* **464**: 674-5.

their financial investment.[144] The 'hype cycle' consists of a curve that describes the 'visibility' of a technology through time, with the intention of helping investors to decide when to invest according to their 'individual appetite for risk'. It begins with a 'peak of inflated expectations' that are generated by an apparent technological breakthrough leading to some early successes and accompanied by significant publicity. Then, as the technology later fails to live up to its early promise, its visibility declines into a 'trough of disillusionment', a critical period in which it may be kept afloat only by surviving early adopters, before new generation products can be generated, and understanding and applications gradually spread (the 'slope of enlightenment'), until a point is reached at which mainstream adoption begins to take hold (the 'plateau of productivity').

2.33 Giving priority to visions of particular biotechnology outcomes – of fully realised conjunctions of knowledge, practice, products and application, and of their place in the imagined future state of the world that they help to make possible – tends to have the two significant effects. Firstly, it 'foreshortens' perceptions of the timescale for the realisation of benefits.[145] Secondly, it 'tunnels' both technology policy and social policy to the detriment of both. It does this, on one hand, by narrowing the way that technology is appreciated to an assessment of its ability to deliver specific outcomes rather than its broader, albeit largely unforeseeable, potential; secondly, it narrows the consideration of the possible ways of achieving social ends to expectations placed on particular technologies. For example, if the 'vision' is to develop third generation biofuels to mitigate climate change, then there can be a tendency to see the benefits of these biofuels *only* in terms of their effect on climate change (and not in relation to other things such as their potential benefits to non-fossil fuel rich economies, even if they do not actually limit global warming). On the other hand, it is not *only* the development of third generation biofuels that can mitigate climate change, and the question of how available resources should be distributed between different approaches is an important one strategically, which may be significantly foreclosed once a dominant vision takes hold. As well as under-representing the complexity and contingency of the innovation process, such 'foreshortening' and 'tunnelling' of expectations may also limit the appreciation of the opportunities for governance and control.[146]

Imported technological visions

Future visions

2.34 One of the ways in which attitudes to prospective technologies are construed is in terms of the kind of world that technological developments may bring about. These commonly incorporate features such as longevity, health into old age, free electricity or power, and inexpensive consumption, with corresponding dystopias, such as decimation by mutant pandemic viruses or the emergence of a 'genetic underclass'. This kind of anticipation may be called the 'sociotechnical imaginary' or 'technoscientific imaginary'.[147] Such imaginaries represent

[144] See, for example: Gartner (2012) *Hype cycles*, available at: http://www.gartner.com/technology/research/methodologies/hype-cycle.jsp. Other models are discussed in Brown N and Michael M (2003) A sociology of expectations: retrospecting prospects and prospecting retrospects *Technology Analysis & Strategic Management* **15**: 3-18.

[145] See: Williams R (2006) Compressed foresight and narrative bias: pitfalls in assessing high technology futures *Science as Culture* **15**: 327-48.

[146] The economist Paul David has argued that 'technological presbyopia' is characteristic of thinking about the microeconomics of biotechnology and other emerging technologies, and accounts substantially for 'productivity paradox': the well-observed phenomenon of fully-realised technologies failing to demonstrate expected impact. He has stated that: "[s]ufferers lose a proper sense of the complexity and historical contingency of the processes involved in technological change and the entanglement of the latter with economic social, political and legal transformations." See: David PA (1989) Computer and dynamo – the modern productivity paradox in a not-too-distant mirror, in *Technology and productivity: the challenge for economic policy* OECD (Editor) (Paris: OECD, 1991), p317. We return to the theme of economic expectations and their influence on public and commercial policy in Chapters 7 and 9.

[147] The phrase 'sociotechnical imaginary' is associated with the work of Sheila Jasanoff (see, for example, Harvard Program on Science, Technology and Society (2012) *The Sociotechnical Imaginaries Project*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries); others use the phrase to mean the ways in which "dissatisfactions with social reality and desires for a better society are projected onto technologies as capable of delivering a potential realm of completeness" See: Lister M, Dovey J, Giddings S, Grant I and Kelly K (2009) *New media: a critical introduction* (New York: Routledge), p60. For resources on the concept of the 'technoscientific imaginary', see: Harvard Program on Science, Technology and Society (2012) *Imagination in science and technology*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries/i.ant/imagination-in-science-and-technology.

prospective technologies from particular perspectives that rely on assumptions (which we discuss under the rubric of 'framing' in Chapter 3) drawn from outside technology, for example from cultural traditions and moral commitments. These range from the perspectives of 'transhumanism', to those of groups opposed to the morally 'dehumanising' social consequences of certain forms of technological development,[148] and may be tied up with social and political objectives such as local or national self-sufficiency, or globalisation.

2.35 The sociotechnical imaginaries associated with decision-making processes for biotechnologies are rarely fully, clearly or consistently articulated. This can lead to an obvious problem: where people conceive of and evaluate prospective technologies as elements within their own personal understandings and visions of the future, the possibility of open debate about common social objectives is diminished. This is especially the case where such decision making impinges on the interests of particular individuals or groups. Where these underlying beliefs and understandings are not articulated, general questions about how a technology can improve social conditions may be replaced by questions relating to discrete issues of cost, safety, ease of implementation, usefulness, impact, etc, which appear to have determinate answers, although these 'answers' add up, collectively, to a vision of the future that has not been debated and may be significantly less desirable to some than to others.[149]

Procedural narratives

2.36 The presentation of particular biotechnologies is often set in the context of grander narratives. Synthetic biology has been described as "the third industrial revolution"[150] and references to previous, economically important technologies are offered as precedents to encourage or justify commercial and political investments. For example, a Royal Academy of Engineering report on synthetic biology states that "many commentators now believe that synthetic biology has the potential for major wealth generation by means of the development of major new industries, much as, for example the semi-conductor did in the last century".[151] This alludes to a very common assertion: that while the 20th Century was 'the age of physics', the 21st Century will be 'the age of biology'.[152]

2.37 These grander narratives can be seen mutually reflected in papers and research proposals, science policy documents and science journalism. A notable feature of these narratives is the use of a number of recurring metaphors, many taken from information technology. In discussions of both synthetic biology and stem cell biology, for example, there is frequent appeal to the idea of "reprogramming" cells.[153] The widely publicised experiment referred to above, in which the DNA of a *Mycoplasma capricolum* cell was replaced by an entirely synthetic

[148] Transhumanism (in this sense) is an ideology that valorises the transformation of the human condition through technologies, for example, to promote life extension, cognitive and physical enhancement. See: Bostrom N (2005) A history of transhumanist thought Journal of Evolution and Technology **14**: 1-25. Others see a bias in favour of high technology approaches as technologies as threatening to biodiversity, agriculture and human rights. See, for example, the ETC Group: http://www.etcgroup.org.

[149] A well-known example here is the debate concerning GM crops where (at least during the early stages) the beliefs and approaches underpinning positions on both 'sides' of the debate sometimes appeared obscured, with the public debate itself explicitly focusing on the 'safety' of the crops rather than on the value judgments of the participants (such as the desirability or otherwise of a profit motive, commercial control of genetic resources and views on power dynamics.) See, for example, Wilsdon J and Willis R (2004) *See-through science: why public engagement needs to move upstream*, available at: http://www.demos.co.uk/files/Seethroughsciencefinal.pdf?1240939425, p27.

[150] See: The Royal Society of Chemistry (2009) A third industrial revolution *Integrative Biology* **1**: 148-9.

[151] The Royal Academy of Engineering (2009) *Synthetic biology: scope, applications, and implications* available at: http://www.raeng.org.uk/news/publications/list/reports/Synthetic_biology.pdf.

[152] The current BBSRC delivery plan opens with a particularly explicit example: "The 21st Century will be the age of bioscience. Driven by new concepts and technologies, a biological revolution is unfolding in the same way that advances in physics shaped the early 20th Century and great leaps in electronics and computing transformed our lives over the past 40 years." See: BBSRC (2011) *BBSRC delivery plan 2011-2015: maximising economic growth in the age of bioscience*, available at: http://www.bbsrc.ac.uk/web/FILES/Publications/delivery_plan_2011_2015.pdf.

[153] Gallivan JP (2007) Toward reprogramming bacteria with small molecules and RNA *Current Opinion in Chemical Biology* **11**: 612-9.

genome,[154] has been described as "rebooting" or "changing the operating system" of life.[155] Its creator has himself been quoted as describing this synthetic cell as "the first cell to have its parent be a computer".[156] Computational metaphors are used when synthetic biologists talk about how DNA can be 'decompiled' through sequencing and then 'recompiled' through synthesis.[157] This metaphor is continued when there is discussion of how in the future biological parts will be combined "in the same manner that Linux modules are now combined to make software".[158] These impressions are only heightened by the conscious adoption of language from information technology, in what might be called biology's 'pop culture', such as the references to 'biohackers' and 'open source biology'.

2.38 For many members of the public, expectations of new technology may arise as much from science fiction, films and video games as from science journalism, a phenomenon known as 'cultivation'. Cultivation analysis has shown how exposure to fictional scenarios in the media can condition expectations of the real world.[159] Themes based on radical genetic modification of organisms, human enhancement and cyborgs are widespread throughout both popular and high culture. However, such influences may not only bear on 'the public': it is interesting to consider to what extent these fictional visions may also be translated back into the world of science. In bionanotechnology, the vision of the 'nanobot' in the form of a miniaturised medical robot has a long fictional pedigree,[160] and it has been argued that many of the themes in 'Plenty of room at the bottom' – the 1959 lecture by Richard Feynman, credited by many as founding the field of nanotechnology – were commonplace in the science fiction of the time.[161] The possibility of using synthetic biology to construct "synthetic ecologies" has been explored in the context of a NASA expedition to Mars,[162] following the familiar science fiction narrative of 'terraforming' uninhabited planets (indeed, in this instance, the term was referenced directly). Meanwhile, the dream of bringing extinct dinosaur species back to life, the central conceit of the novel and film *Jurassic Park*, can be found in synthetic biologists' attempts to resurrect the (albeit much more recently extinct) woolly mammoth.[163]

Methodological scepticism

2.39 While folk narratives and descriptive models may reflect *past* experience, when they are projected into the *future* as a way of organising expectations, they may obscure ambiguities and uncertainties that may be significant for decision making and policy. One uncertainty is that, while expectations of emerging biotechnologies vary over time, they also vary between groups and communities.[164] For example, the detailed technical difficulties and uncertainties that scientists and engineers work with on a day-to-day basis may be invisible to policy makers, investors and the interested public.

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[154] Gibson DG, Glass JI, Lartigue C *et al.* (2010) Creation of a bacterial cell controlled by a chemically synthesized genome *Science* **329**: 52-6.

[155] See, for example, Katsnelson A (2010) Researchers start up cell with synthetic genome *Nature*, available at: http://www.nature.com/news/2010/100520/full/news.2010.253.html and Perkel JM (2010) *Synthetic genomics: building a better bacterium*, available at: http://www.sciencemag.org/site/products/lst_20110325.pdf.

[156] Jones M (2010) House Committee hears from Venter, others on synthetic biology *GenomeWeb Daily News* 28 May, available at: http://www.genomeweb.com/house-committee-hears-venter-others-synthetic-biology.

[157] Specter M (2009) A life of its own: where will synthetic biology lead us? *The New Yorker* 28 September, available at: http://www.newyorker.com/reporting/2009/09/28/090928fa_fact_specter.

[158] Maurer SM (2009) Before it's too late: why synthetic biologists need an open-parts collaboration—and how to build one *EMBO Reports* **10**: 806-9.

[159] See: Gerbner G (1998) Cultivation analysis: an overview *Mass Communication and Society* **1**: 175-94.

[160] Nerlich B (2005) From Nautilus to Nanobo(a)ts: the visual construction of nanoscience *Journal of Nanotechnology Online* **1**: 1-19.

[161] See: Milburn C (2008) *Nanovision: engineering the future* (Durham, North Carolina: Duke University Press). However, some scientists find this claim controversial. For further discussion, see: Milburn C (2010) Modifiable futures: science fiction at the bench *Isis* **101**: 560-9.

[162] Langhoff S, Cumbers J, Rothschild L, Paavola and Worden SP (2010) *Workshop report on: 'what are the potential roles for synthetic biology in NASA's mission?'*, available at: http://event.arc.nasa.gov/main/home/reports/CP-2011-216430_Synthetic_Bio.v6.pdf.

[163] Associated Press (2008) Scientists close in on woolly mammoth *Los Angeles Times* 20 November, available at: http://articles.latimes.com/2008/nov/20/nation/na-mammoth20; *Crichton M (1991) Jurrassic Park (New York: Alfred A Knopf)*; Spielberg S (dir.) (1993) *Jurassic Park* (film).

[164] Brown N and Michael M (2003) A sociology of expectations: retrospecting prospects and prospecting retrospects *Technology Analysis & Strategic Management* **15**: 3-18.

2.40 More generally, there is a fallacy to be avoided that arises from a tendency to make specific claims for particular emerging biotechnologies on the basis of general premises. One might, for instance, believe that currently emerging biotechnologies will become very important in the future and lead to significant increases in human welfare. But what one needs to know in a decision context is what the benefits and costs of a particular biotechnology are likely to be. The answer to that question cannot be deduced from the likelihood of benefit from biotechnology in general. There is, however, a tendency to conflate the general promise with the specific promise and to use the general promise as a strong reason to promote specific technologies.

2.41 The overwhelming weight of history of technologies is that they do not conform to prior expectations. This is hardly surprising as there are many more ways of things going off track than there are of keeping to plan. Many possible pathways are abandoned at an early stage or crowded out by alternatives. Of these, of course, we have no experience, which tends to support an optimism bias: correct past predictions that are reinforced by the presence of the facts they predict are more likely to be remembered than incorrect ones that never materialised.[165] The technologies in use today perhaps represent that small proportion of possible conjunctions of knowledge, practices, products and applications that have been selected and retained because they have been successful in delivering benefits, although they may also have crowded out even more promising alternatives. Such counterfactual possibilities, as we noted in paragraph 1.17, are difficult to explore from the perspective of the factual history that we inhabit, but it is not 'anti-science' to assert that a proper evidence-based understanding of why new technologies emerge depends on a rejection of the simplistic view that the techniques that have been widely adopted are the only important ones. They are only *part* of the relevant evidence.

2.42 Those biotechnologies that do survive long-term may follow any number of different development profiles. Some may be rapidly diffused, whereas others could develop quietly and steadily. Others may remain 'submerged', making little progress for long periods, or disappearing altogether. (Xenotransplantation, for example, was the subject of considerable experimental and clinical activity during the mid-20th Century but ran into a number of setbacks[166] and, as a consequence, little work was carried out for approximately ten years from mid-1970s onwards,[167] with significant interest only returning around the turn of the present century.[168]) On the other hand, examples of relatively rapid transformative biotechnologies can be found: IVF might be thought of as one such innovation that, despite initially unsupportive conditions,[169] led to the creation of a new and thriving fertility industry.[170]

2.43 The broader perspective we take here recommends a sceptical approach to claims concerning prospective biotechnologies. However, this scepticism is not a cynicism about the long term value of biotechnologies in general or about the wisdom of supporting biotechnology research. It is a methodological scepticism that questions reasoning from experience – or reasoning from an inappropriately selected class of experiences – about the prospective benefits of *particular* biotechnologies. This scepticism questions, for example, projected timescales for technology development that do not take into account the complexity of the material conditions of innovation and the difficulty of the adaptations needed for a new technology to become fully productive. This scepticism is not intended to undermine support for biotechnology research, development and innovation in general, but rather to make it stronger (in the sense of being better founded). The questions it poses are rather about *how much* support should be given,

[165] See, for example, the work of Tversky and Kahneman on judging frequency and probability: Tversky A and Kahneman D (1973) Availability: a heuristic for judging frequency and probability *Cognitive Psychology* **5**: 207-32.
[166] Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.
[167] Cooper DKC and Groth C-G (2011) A Record of international meetings on xenotransplantation 1988–2010 *Xenotransplantation* **18**: 229-31.
[168] Persidis A (1999) Xenotransplantation *Nature Biotechnology* **17**: 205-6.
[169] See: Johnson MH, Franklin SB, Cottingham M and Hopwood N (2010) Why the Medical Research Council refused Robert Edwards and Patrick Steptoe support for research on human conception in 1971 *Human Reproduction* **25**: 2157-74.
[170] In 1992, when data were first collected on this issue, approximately 14,057 women received IVF treatment in the UK; in 2007 that number was 36,648 after 15 years of fairly steady growth. See: HFEA (2011) *Long-term trends data - patients treated*, available at: http://www.hfea.gov.uk/2585.html.

when compared with other means to further shared social ends; and about how to respond to 'overpromising' or 'overbelieving' in expected outcomes. As such, methodological scepticism is a long-standing feature of reflection on scientific inquiry.

2.44 Of course, methodological scepticism is exacting to both the optimist and pessimist: we should be prepared just as readily to dismiss the likelihood of harms inferred from previous experience as the expectation of benefits. The absence of a good reason to pursue a particular biotechnology trajectory would not constitute a reason for actively resisting it since, by the same argument, we would have no more reason to expect harms than benefits. However, where it is a question of opportunity costs in alternative uses of resources and, potentially, of locking in alternative futures, a more robust manner of choosing is required.

Conclusion

2.45 In this Chapter, we have turned from the achievements, serendipities and unintended consequences of biotechnologies of the recent past to the prospects and vicissitudes of biotechnologies that are currently emerging. Within the fields of nanotechnology, genetic engineering, regenerative medicine and synthetic biology we encounter a mixture of biotechnologies that are in use, in development or that are merely speculative extrapolations of promising scientific discoveries. We noted how expectations about future biotechnologies are influenced by experience, but that this experience is too often drawn from a few successful biotechnologies, sometimes in very different sectors. We argued that great caution needs to be taken when assigning predictive value to such models that simplify the contingencies and non-linearity of emergence and innovation. Visions of an emerged biotechnology are perhaps better understood as functioning as discursive gambits to secure conditions favourable to a particular pathway.[171]

2.46 We have therefore suggested that the correct mode for the appraisal of emerging biotechnologies is a sceptical mode. Such scepticism should not, however, be seen as 'anti-science' but as methodologically responsible. This is for two reasons: first, premature commitment to a technological pathway is likely to be frustrated and could thereby undermine belief in the value of research; second, setting up a particular outcome as a criterion of success, and organising resources and processes around this may miss broader benefits of research or prevent the balanced appraisal of alternatives. This, of course, both leads back into and deepens the dilemma with which we started: it is no longer just about confronting a decision to commit to one technological pathway at a point before sufficient information is available, but rather about how to balance commitments among a potentially large variety of incommensurable alternatives, none of which may appear obviously preferable.

2.47 A task of this Report is therefore to define modes of decision making that avoid the 'foreshortening' and 'tunnelling' that comes of misrepresenting the complexity of the development and innovation context and the possibility of alternative pathways. To do so is to open up new opportunities for ethical reflection that lie outwith dominant narratives linking prospective biotechnologies and social objectives. So far, we have been largely concerned with descriptive questions about the nature and process of emergence and how it is represented. In the next Chapter, we will begin to consider how normative questions of value enter into the governance of emerging biotechnologies.

[171] "Imagined futures help justify new investments in S&T; in turn, advances in S&T reaffirm the state's capacity to act as responsible stewards of the public good. Sociotechnical imaginaries serve in this respect both as the ends of policy and as instruments of legitimation." See: Harvard Program on Science, Technology and Society (2012) *The Sociotechnical Imaginaries Project*, available at: http://sts.hks.harvard.edu/research/platforms/imaginaries.