Chapter 1

The biotechnology wager

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Chapter overview

Biotechnologies are significant in almost every aspect of human welfare and well-being, from medicine, to food and agriculture, fuel, climate change, and the 'knowledge economy'. The frequent presentation of biotechnology in general as fundamental to future well-being and prosperity suggests that a high stake has been placed in its capacity to fulfil these demanding expectations. However, markedly different views can be taken both about the potential of particular biotechnologies to fulfil these expectations and about how their impacts are to be valued. To illustrate this we consider a range of examples of the achievements, shortcomings and potential of biotechnologies in a range of fields.

We characterise the emergence of biotechnologies as the bringing together of knowledge, practices, products and applications. We note that this process does not conform to a consistent model, that it is poorly understood historically and difficult to control in the present. The contingency of this process suggests that it is appropriate to pose questions about the value of biotechnologies in terms of opportunity costs in order to reveal the assumptions and mechanisms of emergence and identify possible sites of control.

We shift perspective from the emergence of biotechnologies to the conditions in which biotechnologies emerge and distinguish a material context of constraints and conditions, and a discursive context of debate and deliberation in which the material conditions are set.

We describe processes by which technologies adapt to their material context, processes that can 'lock in' technological forms and 'crowd out' others. We describe a dilemma of technology control (the 'Collingridge dilemma') in which decisions taken in the absence of evidence can lead to 'locked in' technological forms that may turn out to have undesirable or suboptimal social consequences.

The biotechnology wager

1.1 The future of human well-being has never seemed more entwined with the choices we make about technologies. Throughout modern history, technology has been at the heart of advances in agriculture, medicine and industry that have seen unprecedented growth in global population and rises in life expectancy and standards of living. In the present century, biotechnologies have emerged as a source of potentially transformative innovations. Experience shows that the same technologies that deliver substantial benefits may also bring unintended consequences, both direct (like antibiotic resistance) and indirect (like loss of biodiversity or accentuated inequalities, both within and between nations).[1] Nevertheless, belief in the potential of biotechnologies for endless progress remains powerful, governing substantial financial and political investment. In order for more people to enjoy longer, healthier, richer and more comfortable lives, it is as if we have – collectively – made a wager on the technologies of the future supplying the means continuously to outrun the costs of consumption and growth.

1.2 This 'biotechnology wager' has both a strong and a weak form. In its weak form it amounts to betting on biotechnologies to deliver future benefits of a kind or to a degree that could not be achieved by alternative approaches. Should this bet miscarry, it would represent a setback in terms of wasted resources and foregone opportunities. In its strong form, it embodies the belief that global challenges such as climate change, food and fuel security and pandemic disease, that exist in part because of the global diffusion and success of past technological advances, have 'locked in' a dependency not only on the continuing performance of existing biotechnologies but *on endless progress in biotechnologies* for the preservation even of existing standards of living. This amounts to a wager on biotechnologies providing remedies for the consequences of past and present use of technology while, at the same time, meeting the challenges of ever increasing consumption and novel threats. Such a wager offers a reason to defer action to address current challenges, inequalities and threats in the anticipation of a future technological solution.[2] Whether we accept the necessity of the wager in its strong or weak

[1] European Environment Agency (2001) *Late lessons from early warnings: the precautionary principle 1896-2000*, available at: http://www.eea.europa.eu/publications/environmental_issue_report_2001_22. Unintended consequences may be both good and bad and, indeed, ambiguous. Increasing global food production has supported increasing population, which has led to further pressure on resources.

[2] This point is made strongly by the economist Paul David: "…it may be a functional response on the part of modern industrial democracies to direct the energies of society away from redistributive struggles and towards the cooperative conquest of the 'endless frontier' of science and its commercial exploitation through technological research and development." David PA

forms, or the faith in limitless progress that it represents, will depend on how we view the challenges we currently face and the alternative responses available.

1.3 If the notional 'biotechnology wager' describes our current commitment to advances in biotechnology, we might reasonably ask how such a wager could come to be made. For example, is it a conscious decision of one or more technologically advanced societies, albeit a decision whose consequences may also bind those in other parts of the globalised world? Is it a decision that enjoys a democratic mandate or an arrangement reached between political, industrial and scientific elites? Is it a conscious decision of anyone at all, or simply the cumulative consequence of many uncoordinated acts, the 'invisible hand' of market forces? This question of how the biotechnologies we end up with come to be determined – and of how they should be determined – by whom, and in relation to what values and criteria, is the central question of this report.

Bio-optimism and bio-pessimism

1.4 In all of the fields in which biotechnologies may play a role – climate, food, energy, medicine, and the economy among them – we encounter both utopian and dystopian visions. The emerging field of synthetic biology, for example, has been compared to the 'green revolution' in the mid-20th Century and the 'information revolution' that followed it. Compared to the physical sciences, scientific understanding in the biosciences during the last few decades has achieved a very great deal in a very short time. On the other hand, *useful* biotechnologies have, so far, been much slower to appear and less transformative than public, policy makers and investors may have hoped or expected. External investment has moved away from the sector, business models have been thrown into turmoil and theories of innovation have been re-examined.[3]

1.5 As well as uncertainty about the likely scale (or timescale) of the impacts of prospective biotechnologies, there may also be significant disagreement about the nature and desirability of the impacts. Experience suggests that few benefits are obtained without some cost, and that few achievements are secured without repercussions. This suggests two axes against which attitudes and expectations concerning prospective biotechnologies may be plotted: those of impact (ranging from trivial to transformative) and benefit (beneficial to harmful). As biotechnologies are implemented and diffused, and evidence begins to accumulate, these expectations may be confirmed or confounded and the majority of evaluations may converge on a particular point, although this is by no means necessarily or inevitably the case.

1.6 Ambivalence about prospective biotechnologies may often give way to polarised views when key questions about technology are posed as if what was at stake was a matter of saying 'yes' or 'no' to some fixed idea of technological advance, rather than considering alternative directions for progress.[4] The biotechnology wager, strong or weak, represents a position taken up in one quadrant of a matrix of possible attitudes to prospective biotechnology. However, it is likely that examples of all these attitudes can be found without too much difficulty in relation to almost any prospective biotechnology.

(1991) Computer and dynamo – the modern productivity paradox in a not-too-distant mirror, in *Technology and productivity: the challenge for economic policy* (Paris: OECD), p317.

3 On investment, see Chapter 9. For an assessment of the contribution of biotechnology in the field of pharmaceutical innovation, see: 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.

4 See: Stirling A (2011) From enlightenment to enablement: opening up choices for innovation, in *The innovation for development report 2009-2010*, López-Claros A (Editor) (Basingstoke: Palgrave Macmilan).

Box 1.1: Attitudes to biotechnology

Attitudes towards biotechnologies vary considerably between individuals and over time. Different attitudes may persist in relation to both prospective biotechnologies, and to technologies that are already implemented and well diffused, where evidence relating to them is available. Indeed, attitudes may continue to vary as new evidence and understandings emerge. The examples given below are therefore provisional, and simply suggest where the bulk of opinions appear to converge at the present time.

High impact, Positive net benefit Biotechnologies about which opinion converges in this quadrant are those considered most socially desirable; these may include important 'public goods', for example vaccination.[a]	**Low impact, Positive net benefit** Biotechnologies about which opinion converges in this quadrant may be socially desirable but are more likely to be privately valued (some medicines, for example[b]).
High impact, Negative net benefit Where opinion converges in this quadrant biotechnologies are likely to involve significant public harms or risks. These may not be apparent at an early stage so technologies may be widely implemented before they are recognised. Examples outside biotechnology include chlorofluorocarbons (CFCs) and asbestos.[c]	**Low impact, Negative net benefit** Comparatively poorer performance than alternative; they may tolerated owing to a greater value being placed on the exercise of individual freedom (for example, technologies on the borderline of 'health care'[d]).

[a] The impact and positive benefit of vaccines is well documented.[5] However, although vaccination is generally considered to have a positive net benefit, this is contested by some groups (especially in relation to compulsory vaccination).[6]

[b] Medicines for certain cancers rejected on the basis of cost-effectiveness (such as by the National Institute for Health and Clinical Excellence (NICE) in the UK) might also fall into this category when they are deemed to have too little benefit in comparison to their cost-per-patient – i.e. if life is extended by a marginal amount.[7]

[c] Both CFCs and asbestos, about which the balance of opinion has now moved fairly decisively into this quadrant, were very effective for their intended use but turned out to have extremely harmful and widespread collateral consequences.

[d] It has been suggested that some applications of genetic screening (pre-implantation,[8] preconception,[9] personal genetic profiling[10]) may, under some perspectives have negative benefit (raising anxieties unnecessarily, involving medical procedures with no clear benefit, giving false confidence, causing unnecessary pressure on public health services, etc.). However, there is usually sufficient ambiguity about the harms that the infringement of personal and commercial freedom that would be involved in banning those technologies argues against prohibiting them. This tolerance may be important – it is worth recalling that the balance of views about many 'disruptive' technologies may be initially fall into this quadrant.

The biotechnology balance sheet

1.7 Examples of genuinely harmful technological impacts from the past should be hard to find as markets, governance and regulation should weed them out before significant harmful effects accumulate. However, it may take some time before undesirable effects are recognised and

[5] "The impact of vaccination on the health of the world's people's is hard to exaggerate. With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction or population growth." Plotkin SL and Plotkin SA (2004) A short history of vaccination, in *Vaccines*, Plotkin SA Orenstein WA and Offit PA (Editor) (China: Saunders Elsevier), p1. See also: Payette P and Davis H (2001) History of vaccines and positioning of current trends *Current Drug Targets - Infectious Disorders* **1**: 241-7.

[6] For a discussion of attitudes to vaccines and vaccination programmes, see: Larson HJ, Cooper LZ, Eskola J, Katz SL and Ratzan S (2011) Addressing the vaccine confidence gap *The Lancet* **38**: 526-35.

[7] See, for example, the situation in the UK with regard to the drug everolimus: NICE (2012) *Everolimus for the second-line treatment of advanced renal cell carcinoma*, available at: http://publications.nice.org.uk/everolimus-for-the-second-line-treatment-of-advanced-renal-cell-carcinoma-ta219, and BBC Online (2011) *NICE rejects kidney cancer drug everolimus*, available at: http://www.bbc.co.uk/news/health-13115961.

[8] Brown R and Harper J (2012) The clinical benefit and safety of current and future assisted reproductive technology *Reproductive Biomedicine Online* **25**: 108-17.

[9] Human Genetics Commission (2011) *Increasing options, informing choice: a report on preconception genetic testing and screening*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/Increasing%20options,%20informing%20choice%20-%20final.pdf.

[10] The issue of genetic profiling has also been subject to considerable and recent debate. See, for example, 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; Human Genetics Commission (2003) *Genes direct*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/genesdirect_full.pdf and Human Genetics Commission (2007) *More genes direct*, available at: http://www.hgc.gov.uk/UploadDocs/DocPub/Document/More%20Genes%20Direct%20-%20final.pdf.

begin to tip the balance in favour of modified or alternative technologies (or stimulate the search for alternatives). In framing the question of how technologies come to be developed and brought into use it is instructive to consider how existing technologies may accumulate undesirable side-effects and how the beneficial and unwanted effects are distributed. To assess the impetus behind the biotechnology wager, it will help to understand the extent to which further technological 'fixes' are necessitated by prior use of earlier technologies. We cannot explore this question in detail in every field of biotechnology but we will now consider some examples of the achievements, collateral effects and current possibilities of biotechnology that suggest a level of commitment to the biotechnology wager.

Food security

1.8 A range of technologies, including chemical pesticides, fertilisers, irrigation and plant breeding, have transformed agricultural food production since the 1940s, in particular through technology transfer to developing countries (the 'green revolution'). Artificially bred high-yielding varieties of wheat, rice and maize have been central to this revolution. A more than doubling of global food production in the past 40 years has been achieved despite only an eight per cent increase in the use of land for agriculture in the same period.[11] However, the long term sustainability and social impacts of production methods have come increasingly into question. The very technologies that have made historic productivity increases possible (for example, the Haber-Bosch process to 'fix' nitrogen – converting atmospheric nitrogen to ammonia – for fertiliser) have been accompanied by an accumulation of undesirable collateral effects such as increases in water and air pollution, rising greenhouse gas levels, and the reduction of biodiversity.[12] At the same time, the dependency on fixed nitrogen has been substantially 'locked in' by the need to feed rising populations (particularly populations dependent on some of the least productive land).[13] Biotechnology offers potential responses through the possibility of genetically engineering food crops to increase yield and adapt to new or altered environments, the use of advanced genetics to enhance conventional breeding systems without direct manipulation of the genome, or the development of new synthetic biology technologies to enable the 'designing in' of multiple genetic traits (higher yields, drought and disease tolerance).[14] However, biotechnology is only one element of a potential response to global food security. As such, it must be assessed alongside a range of different scientific, institutional and organisational innovations (like changing the crops under cultivation, 'open source' supply chains, ecological farming practices and support for participatory farmer-led plant breeding).[15]

Energy security

1.9 Demand for energy is predicted to rise by a third between 2010 and 2035, a demand that cannot be met by climate-damaging carbon-intensive technologies if there is to be any prospect of limiting global warming.[16] While the most important contribution to reaching energy security and climate goals is reduced consumption, energy efficient and low emission technology are

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[11] Beddington J (2009) *Food, energy, water and the climate: a perfect storm of global events?*, available at: http://www.bis.gov.uk/assets/goscience/docs/p/perfect-storm-paper.pdf, citing Parry ML, Canziani OF, Palutikof JP, van der Linden PJ and Hanson CE (Editors) (2007) *Climate change 2007: impacts, adaptation, and vulnerability* (Cambridge: Cambridge University Press).

[12] Erisman JW, Sutton MA, Galloway J, Klimont Z and Winiwarter W (2008) How a century of ammonia synthesis changed the world *Nature Geoscience* **1**: 636-9.

[13] Galloway JN and Cowling EB (2002) Reactive nitrogen and the world: 200 years of change *AMBIO: A Journal of the Human Environment* **31**: 64-71.

[14] 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.

[15] Leach M, Scoones I and Stirling A (Editors) (2010) *Dynamic sustainabilities: technology, environment, social justice* (London: Earthscan).

[16] See: International Energy Agency (2011) *World energy outlook 2011: executive summary*, available at: http://www.iea.org/Textbase/npsum/weo2011sum.pdf. The figure for the rise in demand for energy is based on 1.7 billion population growth and 3.5 per cent global average gross domestic product (GDP) growth over the period, although acknowledging the global economic situation, they estimate that lower short term growth will have only a marginal effect. New approaches are required because four-fifths of energy related carbon dioxide emissions permissible by 2035 (to hit the 2˚C global temperature increase target) are already accounted for by existing infrastructure.

inevitably called for. Biotechnologies may contribute to this in a number of important ways. As all of the projected net increase in demand for oil is accounted for by personal mobility and freight in emerging economies, the engineering of new generations of biofuels that avoid the harmful impacts on land use characteristic of 'first generation' biofuels is strongly favoured, although the technological means by which this could be achieved is currently uncertain.[17] Perhaps the most important contribution of biotechnologies, however, may lie in their capacity to help to make production processes in a variety of applications, significantly less energy intensive.[18]

Biomedicine

1.10 Advances in biomedicine contributed – alongside improved sanitation, nutrition and living and working conditions – to a steady rise in life expectancy and general standards of physical well-being throughout the 20th Century in industrialised countries.[19] Successes in preventing and treating communicable diseases have, in developed economies, shifted the focus onto non-transmissible diseases, diseases of lifestyle and old age, obesity, cancer, heart disease and dementia. While advances over the last century, such as antibiotics, have meant that previously life-threatening infections are now routinely survivable, widespread use of antibiotics in human and veterinary medicine, and in routine livestock production, has been identified as a significant cause in the rise of antibiotic and multi-drug resistant bacteria.[20] At the same time, further challenges have arisen through the resurgence of malaria,[21] pandemic strains of influenza, and HIV. Biotechnologies offer some important strategies to address all these challenges, although in some cases they face substantial institutional, economic and regulatory hurdles, in addition to biological complexity. For example, the realisation of more 'personalised' medicine is far from straightforward not least because a key element, the pharmaceutical industry, is currently struggling to find a business model that would support such a transformation in medicine.[22] Furthermore, it remains the case that market incentives appear to foster greater attention to disorders of most concern among rich populations, than to treating many severe conditions suffered by the global poor.[23]

The economy

1.11 High expectations are placed on bioscience and biotechnology as a major contributor to the economy.[24] The financial crisis that began in the United States and Western Europe in 2007-8, and the subsequent recession, has focused attention on the search for potential new drivers of economic growth. Both the UK and EU responses to the crisis stress the importance of research and development.[25] However, how to translate national investment in research and

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17 Nuffield Council on Bioethics (2011) *Biofuels: ethical issues*, available at: http://www.nuffieldbioethics.org/biofuels-0.

18 See, for example, the use (and modification) of particular enzymes in the commercial-scale production of some antibiotics and 'advanced' biofuels: Davidson S (2008) Sustainable bioenergy: genomics and biofuels development *Nature Education* **1**; DSM (1999) *DSM to invest NLG 15 million in enzyme plant in Delft (Netherlands)*, available at: http://www3.dsm.com/newsarchive/1999/~en/g_246end31_en.htm. See also: OECD (2011) *Industrial biotechnology and climate change: opportunities and challenges*, available at: http://www.oecd.org/sti/biotechnologypolicies/49024032.pdf, p19.

19 See: Riley JC (2001) *Rising life expectancy: a global history* (Cambridge: Cambridge University Press), p51ff.

20 Russell E (2011) *Evolutionary history: uniting history and biology to understand life on Earth* (Cambridge: Cambridge University Press).

21 Malaria Foundation International (2012) *Resurgence of malaria*, available at: http://www.malaria.org/index.php?option=com_content&task=view&id=130&Itemid=32.

22 In the meantime, some of the challenges of global scope (e.g. malaria) are being addressed by new non-commercial initiatives such as that of the Bill and Melinda Gates Foundation. See: PATH Malaria Vaccine Initiative (2012) *About us*, available at: http://www.malariavaccine.org/about-overview.php.

23 For example, Médecins Sans Frontières and the 'Drugs for Neglected Diseases Initiative' have noted that, out of 1,556 medicines developed between 1975 and 2004, only 18 (21, if malaria and tuberculosis are included) were indicated for diseases that mainly affect people in developing countries. See: Chirac P and Torreele E (2006) Global framework on essential health R&D *The Lancet* **367**: 1560-1.

24 See: 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, where it is stated, for example that "[l]ife sciences will continue to be vibrant in the UK and will be a *key contributor to sustained economic growth*.", p6. (Emphasis in original.)

25 The second EU 2020 target (part of the EU's growth strategy for the second decade of the new millennium) states that three per cent of EU GDP (public and private combined) is to be invested in R&D/innovation (see: European Commission (2011) *Europe 2020 targets*, available at: http://ec.europa.eu/europe2020/targets/eu-targets/index_en.htm) This is strikingly

development into safe, desirable, beneficial and profitable products that will primarily benefit that nation is perhaps the single most disputable aspect of research policy. Historically, the fastest growing economies have not been high-income countries with high expenditure in research and development but middle-income countries that are able to grow quickly as a result of imitating the technologies developed elsewhere.[26] Furthermore, even where there appears to be a strong relationship between growth and advanced technology, the pursuit of growth does not address the question of the appropriate aims and orientation for technological progress in any particular sector.[27]

1.12 These examples from different fields show that the path of biotechnology innovation is complex, lengthy, difficult to control and subject to unanticipated consequences. In the following sections we consider what distinguishes the emergence of biotechnologies from the delivery of new products or services, namely, the dynamic relationship between the emerging technology and the conditions of its development and innovation.

Emerging

1.13 The term 'biotechnology' is commonly used, but not always well defined. When we refer to 'a biotechnology' in this report we mean a productive conjunction of knowledge, practices, products and applications. 'Practices' in this sense include both techniques that depend on machinery or automated procedures as well as voluntary human actions ('standard operating procedures'). 'Products' include services and consumables as well as tangible and durable objects; these may be intermediate products, for example, machines to be used in production. If a biotechnology is a conjunction of this kind, then in a very simple sense 'emerging' is the *assembling* of this conjunction.[28] Assembling in this sense is always subject to conditions and externalities that both affect it and that it affects. In examining how biotechnologies emerge, we are primarily concerned with the interplay between the potentialities and limitations inherent in the technology, and the conditions that lead to or obstruct the innovation of that technology in a particular place and at a particular moment in history.

1.14 This assembling, or emergence, does not necessarily follow an ordered and linear path from 'science', through applied research and innovation to widespread use, or perhaps may do so only in unusually controlled conditions. The path of emergence may begin at almost any point and rarely runs straight. Some of the most ambitious initiatives in emerging biotechnologies, such as 'BioBricks'® in synthetic biology[29] and the 'virtual patient' in personalised medicine, for example, were driven by applications-focused engineering and information technology initiatives (respectively) rather than by research in biological science. Equally, the assembling does not necessarily require the injection of new knowledge: 'emerging biotechnologies' may emerge as the result of a convergence between well understood pre-existing techniques that may only become possible when certain external conditions fall into place. This is to say that the emergence of a biotechnology:

- engages different social actors and groups in unique configurations (scientists, engineers, policy makers, publics, etc.);

conspicuous as the only 'input target' out of the five targets (the four others being outcome targets). UK spending was 1.86 per cent GERD in 2009 (see: European Commission (2012) *Europe 2020 in the United Kingdom*, available at: http://ec.europa.eu/europe2020/europe-2020-in-your-country/united-kingdom/index_en.htm).

[26] Edgerton D (2008) *The shock of the old* (London: Profile); see also Chapter 7.

[27] Stirling A (2009) *Innovation, sustainability and development: a new manifesto – direction, distribution and diversity! Pluralising progress in innovation, sustainability and development*, available at: http://anewmanifesto.org/wp-content/uploads/stirling-paper-32.pdf.

[28] In our view, this description as an 'assembling' captures better than 'emerging' the active endeavour involved both in developing biotechnologies and in establishing the conditions that facilitate and govern such development, but we retain the established term to avoid confusion.

[29] See paragraph 2.19.

- is orientated towards solving problems and delivering concrete applications (but capable of capitalising on serendipities);
- draws on knowledge and technical expertise from a variety of fields (producing *ad hoc* productive configurations); and
- is influenced by social, as well as technical, conditions and implications.[30]

1.15 Looking back at innovations of the past, it is easy not to recognise the contingency of the technological pathways that have led to the present.[31] Our understanding of where, why and how novelties emerge is often strongly affected by theoretical models that fail to reflect the great diversity, uncertainty and serendipity of novelty generation.[32] These processes are inherently hard to research. Our understanding of them is limited in that most ideas are not developed and most inventions not exploited. More importantly, by focusing only on how technologies fulfil the expectations that are set for them, we may fail to take account of the unexpected consequences, beneficial or harmful, to which they can lead.

Opportunity costs and counterfactuals

1.16 Stepping back from the narrow focus on biotechnologies to look more roundly at the states of affairs that they address brings into view reasons to hesitate in making the 'biotechnology wager'. One of these is that the focus on 'high' technologies might entrench the values of consumerism and exacerbate inequalities in the distribution of benefits and costs. (Consideration might be given instead, for example, to investing greater political attention and economic support in forms of social and organisational innovation that prioritise the needs of the poorest and most vulnerable people.) While emerging biotechnologies may offer significant responses to current and future challenges in a number of sectors, this question of appropriate mix – both among different biotechnological strategies and between biotechnologies and alternative strategies – is an important but under-discussed one for public policy.

1.17 This broader perspective suggests that the current landscape of technologies is not the only one possible.[33] At earlier points in history, but for the particular conjunction of conditions that obtained at the time, other technologies might have developed that could have led to a very different state of affairs in the present.[34] While such reflection cannot tell us what an alternative, 'counterfactual' present might be like had a different path been taken at some significant crossroads in the past, it serves as a reminder that the present is contingent upon a mixture of past conditions and choices. In a similar way, the future is contingent upon a complex set of conditions that are determined or accepted now. This is not to say that these choices or their significance can always readily be seen in advance; but the choices are likely to be unduly restricted if the way we think about emerging biotechnologies is limited to, or framed as, discrete considerations of specific technologies or specific outcomes. Indeed, an overemphasis on

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[30] This mirrors analyses of the more complex ways in which knowledge itself may be produced; see: Gibbons M, Limoges C, Nowotny H *et al.* (1994) *The new production of knowledge: the dynamics of science and research in contemporary societies* (London: Sage) and Nowotny H, Scott P and Gibbons M (2001) *Re-thinking science: knowledge and the public in an age of uncertainty* (Cambridge: Polity Press).

[31] Deuten and Rip examine how recollection applies a *post-hoc* rationalisation to explain the outcomes that actually transpired, in the process, marginalising the contingency and precariousness of the process that led to them: Deuten JJ and Rip A (2000) Narrative infrastructure in product creation processes *Organization* **7**: 69-93.

[32] Edgerton has argued that most histories of technology are actually poor guides to what might happen in the future because they fail to identify what were actually the most important technologies in particular periods, or identify them at all, focusing instead on what was considered most novel, controversial or revolutionary. For example, perhaps one of the greatest transformations in human history, namely the massive increase in land and labour productivity in agriculture in rich countries after 1945 is surprisingly absent from general texts on the period, which instead identify the period with nuclear power, rockets, etc. See: Edgerton D (2008) *The shock of the old* (London: Profile).

[33] Ibid. For a discussion of 'counterfactual history' more generally, see: Bunzl M (2004) Counterfactual history: a user's guide *The American Historical Review* **109**: 845-58.

[34] See, for example, the emphasis on the development (and subsequent dominance, in some quarters) of light-water nuclear reactors as a consequence of prevailing military priorities in the US following the Second World War. See: Cowan R (1990) Nuclear power reactors: a study in technological lock-in *The Journal of Economic History* **50**: 541-67. See also the focus on the possibility that thorium fuel cycle reactors offer an alternative: Galperin A, Reichert P and Radkowsky A (1997) Thorium fuel for light water reactors—reducing proliferation potential of nuclear power fuel cycle *Science & Global Security* **6**: 265-90.

specific technologies, 'golden opportunities' or, 'royal roads', for example, risks making any resistance to specific technological commitments appear to betoken an 'anti-science' or 'anti-technology' prejudice. In fact, resistance to innovation is indispensable, and criticism of novelties valuable, in revealing the diversity of options available and the viability of those alternatives.[35]

1.18 The question of 'opportunity cost', of what is foregone in the attempt to secure a selected benefit, is one that is familiar to economists but too seldom adequately considered in relation to technological commitments. Such consideration may appear difficult because it is usually taken to mean speculating about a range of futures where both the possibility of realising them and the values attached to the realisation are so uncertain. It can, nevertheless, provoke a constructive examination of the conditions that constrain decision making, help to illuminate unquestioned assumptions, and identify a broader range of choices that are available. We therefore make the recommendation – one that has guided our own deliberations – that **commitments to particular technological pathways should be evaluated not only in terms of their expected future impacts but also by comparison to possible alternative pathways; this can help to illuminate obscured assumptions, constraints and mechanisms of the innovation system, and help to identify sites and opportunities for more constructive governance, prioritisation and control**. Guided by this recommendation we now turn our attention to the contextual conditions within which biotechnologies emerge and the role that those conditions play in constraining or opening up possible trajectories of development.

Contingency and its consequences

Material and discursive contexts

1.19 We have seen that the emergence of new biotechnologies may be characterised as a contingent, branching process whereby some possible trajectories are selected in preference to others. Different pathways may be explored simultaneously, although probably not all of those that are possible; sometimes a single approach becomes dominant and others are neglected (although they may be returned to later, especially if conditions change).

1.20 The unfolding of this process is governed by a mixture of intrinsic potentialities and contingent conditions. Intrinsic potentialities will include things like hard physical constraints that limit the viability of a given technology and define its operational parameters. Contingent conditions will include things like institutional structures, networks of communication for the transfer of knowledge between researchers, inputs of funding and investment, allocation of resources, legal constraints and regulatory requirements. Together, these intrinsic and contingent conditions make up what we will call the 'material context' of biotechnology emergence.

1.21 While intrinsic potentialities are a given (even if they are not wholly understood), contingent conditions often fall within the scope of human choice, even if they are not actively chosen. Choices may weave together complex moral and factual judgments as well as subtle attitudes and beliefs, values and dispositions. The context in which these are expressed is a 'discursive context' of discussion, debate and deliberation. Such contexts involve different groups of individuals invested with different kinds of powers. The discursive context provides an opportunity to examine hypothetical or imaginary states of affairs and the values associated with them. However, it is also where decisions are made that alter the material context, for example, decisions to initiate a line of research, allocate funding, and impose legal or other constraints. (How the discursive context itself may come to be structured for particular biotechnology decisions is an important question for this Report that we will address in the next Chapter.)

[35] Edgerton D (2008) *The shock of the old* (London: Profile), p9. Such resistance may even be essential and, whereas it is often left to non-scientists and for this reason risks being politically marginalised, is something that scientists themselves should undertake; see: Edgerton D (2011) In praise of Luddism *Nature* **471**: 27-9.

1.22 The selection of contingent conditions can be highly decisive, particularly where there is significant uncertainty about the technology's potential to deliver effective applications. One might think here of the reasons that different approaches to human stem cell research were pursued in the UK, where research has concentrated on licensed use of human embryonic stem cells (hESC), and in Germany, where destructive human embryo research is unlawful.[36]

1.23 Contingent conditions need not be 'all or nothing': they can exert selective pressures that simply favour or deter, to varying degrees, certain pathways in relation to possible alternatives.[37] Their effects are likely to be aggregate, and within this aggregate, one condition may counteract another. Being multiple, they are often determined by a range of different actors (firms, governments, researchers and others) rather than being controlled by a single, well-informed actor following a consistent strategy. These different actors (or networks or groups of actors) will sometimes have significantly different objectives, and different beliefs and understandings of the technological options. A lack of coordination – or outright opposition – can create strong and sometimes counterproductive pressures.[38] Some important conditions may not therefore be the result of active 'decisions' at all, either because they are not the intentional outcome of a single decision (but the unintended consequences of a set of discrete interventions taken without a view to their collective effect) or because they are the result of omissions.[39]

Technological 'lock-in'

1.24 Although some decisions in the global pathway of technology development may be contingent upon sometimes very minor influences, once a pathway is established, technologies can easily become entrenched or 'locked in'. Central to the explanation of technological 'lock-in' is the idea that specific technological pathways, once embarked upon, become progressively difficult and costly to escape. In economic terms, this is generally attributed to the mutual adaptation of the technology itself and market conditions, learning effects and increasing returns to scale, etc.[40] Technologies may also acquire 'momentum' from the feedback between technology and society through, for example, lifestyle adaptations to particular products.[41]

1.25 The adaptations and accommodations that 'lock-in' technologies also, of course, bring gains in terms of efficiency and utility. However, this may mean that the innovation conditions faced by new technologies are most likely to be conservative, since it is probable that they will have been aligned so as to make the most effective use of incumbent technologies. Even where – rather than competing with existing technologies, new technologies open up an entirely new market or

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[36] Research in the UK has focused primarily on deriving hESC subject to the Human Fertilisation and Embryology Act 1990 (as amended); in Germany, owing to the interpretation of constitutional prohibitions in the Basic Law (Grundgesetz) and s.2 of the Embryo Protection Act 1991 (Embryonenschutzgesetz) it has focused on imported lines (pursuant to the Stem Cell Act 2002 (Stammzellgesetz) (as amended)), somatic stem cells and induced pluripotent stem (iPS) cells. Notwithstanding the permissive legal environment in the UK, research may nevertheless come to be affected by the possibilities of patenting, and therefore successfully commercialising, products in the light of the European Court of Justice's finding in *Brüstle v. Greenpeace eV* (Case C-34/10), 18 October 2011.

[37] For example, tax incentives might be used to encourage particular activities in specific places: scientific and technological endeavour generally might be encouraged (as under the UK Government's research and development relief for corporation tax) or specific disciplines might be given favourable terms (such as New York City's biotechnology tax credit). See: HMRC (2012) *Research and development (R&D) relief for corporation tax*, available at: http://www.hmrc.gov.uk/ct/forms-rates/claims/randd.htm; NYC Government (2012) *Answers to the most frequently asked questions about biotechnology credit against the general corporation tax and the unincorporated business tax*, available at: http://www.nyc.gov/html/dof/html/pdf/10pdf/biotech_faq.pdf.

[38] See paragraph 7.11 below, for an example whereby government investment intended to leverage private sector R&D investment apparently had the opposite effect.

[39] For example, human reproductive cloning research was allegedly pursued for some time in Italy, owing to that country's reticence in legislating for reproductive technologies; see: BioNews (2004) *Antinori restates clone claims*, available at: http://www.bionews.org.uk/page_11939.asp.

[40] See: Boas TC (2007) Conceptualizing continuity and change: the composite-standard model of path dependence *Journal of Theoretical Politics* **19**: 33–54).

[41] The theory of 'technological momentum' was developed by Thomas Hughes in the late 1960s. See: Hughes TP (1969) Technological momentum in history: hydrogenation in Germany 1898-1933 *Past & Present* **44**: 106-32.

range of possibilities – they may still suffer disadvantage through a lack of conducive environmental conditions.[42]

1.26 Conditions in the innovation environment may even ensure that there may only be space for one technological 'winner' that may come to dominate a field of practice to the extent that potential alternatives are 'crowded out'.[43] This winner, however, need not be the 'best' overall candidate from all perspectives,[44] if successive rounds of selection operate according to different criteria (technical, political, social, economic, etc.).

An innovation dilemma

1.27 A dilemma facing a society that seeks to govern innovation is that often the consequences of introducing new technologies can only be fully understood once the technology is in use; by that time, however, it may be too late to change course. This difficulty was expressed by the British social philosopher David Collingridge in the form of a 'technology control dilemma'.

Box 1.2: Collingridge's technology control dilemma

Efforts to control technology face the following dilemma:

1 Limited predictability: "understanding of the interactions between technology and society is so poor that the harmful social consequences of the fully developed technology cannot be predicted with sufficient confidence to justify the imposition of controls."

2 Limited power: "by the time a technology is sufficiently well developed and diffused for its unwanted social consequences to become apparent, it is no longer easily controlled. Control may still be possible, to some degree but it has become very difficult, expensive and slow."[45]

1.28 As presented, the dilemma focuses on avoiding undesirable but unforeseen social consequences of technology, but it might equally apply to the problem of securing the most desirable benefits. The power of the dilemma arises from the fact that the consequences of decisions about what technological trajectories to pursue potentially 'lock in' a given technology and simultaneously 'crowd out' alternatives in a context in which switching paths may set back the achievement of a benefit by decades.[46] Of course, biotechnology innovation has its own special features that are different from the military and industrial technologies considered by Collingridge but the essential point about the need to make commitments in the absence of relevant evidence remains pertinent.

1.29 It is important not to overstate the implications of the Collingridge dilemma. It does not imply that rigorous social appraisal of alternative technological trajectories is impossible at an early stage. (Collingridge's own argument explicitly highlighted the need for greater efforts in this direction.) It does, however, serve to emphasise the sobering predictive challenges that accompany

[42] This may account for the 'productivity paradox' when computers first became widely available, i.e. the seeming disconnection between advances in computing power (and implementation of computing power) and the concurrent slow growth in productivity. (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)). As we suggest in Chapter 8, the absence of a regulatory system for novel biotechnologies does not necessarily give them an advantage over regulated technologies, and adapting an existing system can be difficult.

[43] However, potential alternatives need not always be entirely 'crowded out', as evidenced by the example of electricity generation. Here, strategic vision can deliberately act *against* technically or economically dominant technologies crowding out alternatives. See: Stirling A (2010) Multicriteria diversity analysis: a novel heuristic framework for appraising energy portfolios *Energy Policy* **38**: 1622-34. For a biotechnological example, one might consider the use of 'primer walking' and 'shotgun' DNA sequencing (two techniques used concurrently for (broadly) the same purposes, which are now being replaced with 'next generation' high-throughput sequencing.)

[44] There is some dispute in the economics literature about how far the concept of lock-in can explain apparent market failure to select the best alternative. See, for example: Liebowitz S and Margolis SE (2010) *The troubled path of the lock-in movement*, available at: http://ssrn.com/abstract=1698486.

[45] Collingridge D (1980) *The social control of technology* (Milton Keynes: The Open University Press), pp17-8.

[46] "What happens is that society and the rest of its technology gradually adjust to the new technology, so that when it is fully developed any major change in the new technology requires changes in many other technologies and social and economic institutions, making its control very disruptive and expensive". Ibid.

genuinely novel technologies and urges greater caution, responsibility and accountability in policy decisions about such technologies. It also places a premium on effective social and institutional learning. In particular, there is nothing about Collingridge's important insight into the difficulties of acting with incomplete knowledge that prevents scrutiny of the aims and interests that animate research, development and innovation of emerging biotechnologies.[47] Ignorance of the future means that the problems of absence of evidence may be inescapable, but this also provides the basis of a case for making the governance of emerging biotechnologies more reflective.[48]

Path dependency

1.30 The choices that face a society about what technologies to pursue are rarely as stark as the technology control dilemma suggests. For example, they are seldom about whether to say 'yes' or 'no' to a given technology or, if they are, they are perhaps already coming too late to allow a balanced, unconstrained decision to be made. The decision has been brought to this point, implicitly, because alternatives are already weeded out: the dilemma, if not the technology itself, is already locked in. To engage in a balanced appraisal of opportunity costs it is therefore necessary to consider how the point may be arrived at where this dilemma appears to have become inescapable.

1.31 Sunk costs and market conditions are not the only conditions determining emerging biotechnology trajectories, and perhaps not the most important. Well before the point of innovation, a variety of conditions influence research and development. These conditions include allocation of funding, disciplinary hierarchies and agendas, and research regulation as well as anticipated market response. But the constraints extend also into the discursive context, with intellectual constraints operating as blinkers at critical decision stages. Alternative technological pathways may even be difficult to conceive of because knowledge cultures or certain ways of working can limit the ability to imagine a radical alternative.[49] Even where alternative approaches *can* be conceived, they may be strongly associated with visions of alternative future states of affairs that people will value differently. Therefore the way in which different sets of social, institutional and technological conditions are seen as aligning with these envisaged futures means that certain alternatives may be 'crowded out' at an early stage.

1.32 The fact that the conditions that shape emerging biotechnologies may be determined discretely, in different contexts, and in an ordered sequence implicitly creates 'path dependencies', where prior decisions constrain and condition the range of possibilities available at subsequent stages. The order in which these decisions occur, and the groups to which they are reserved, therefore matter importantly, since earlier decisions 'frame' the subsequent questions. Furthermore, the segregation of different decisions into different technical 'types' to be dealt with by different expert groups prevents broader engagement between these technical domains and means that, because of the ordering, priorities and interests of certain technical elites (scientific, political, industrial) may constrain the effect of other influences. Hence the familiar complaint that ethical reflection is restricted to the conduct and implications of a particular type of research or innovation (i.e. after the scope and nature of the research has been determined) rather than the

[47] For an examination of scrutiny of these areas under conditions of uncertainty, see: 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; Scoones I, Wynne B and Leach M (Editors) (2005) *Science and citizens: globalization and the challenge of engagement (claiming citizenship)* (London: Zed Books).

[48] Stirling A (2008) Science, precaution, and the politics of technological risk: converging implications in evolutionary and social scientific perspectives *Annals of the New York Academy of Sciences* **1128**: 95-110.

[49] See, for example, Dosi's work on the concept of 'technological paradigms'. Dosi draws explicit parallels between his idea of a technological paradigm and Kuhn's concept of scientific paradigms. He notes: "'Technology' [in the view of the framework outlined] includes the 'perception' of a limited set of possible technological alternatives and of notional future developments… a technological paradigm…embodies strong prescriptions on the directions of technical change to pursue and those to neglect… certain specific technologies emerg[e], with their own "solutions" to those problems and the exclusion of other notionally possible ones." Dosi G (1982) Technological paradigms and technological trajectories: a suggested interpretation of the determinants and directions of technical change *Research Policy* **11**: 147-62.

question of whether such research or innovation is appropriate in the first place, particularly in the context of other uses of resources.[50]

1.33 This determination of technological paths through managed decision making in technically defined contexts (where certain sorts of technical expertise are privileged) may therefore reinforce path dependency and make consideration of opportunity costs more difficult. Nevertheless, *just because* segregating and sequencing decision stages in this way can create managed path dependency, it offers an attractive approach to governing the emergence of biotechnologies. As a prescription for technology control it raises two sorts of objections, though. The first, as suggested above, is that it offers the possibility of control at the expense of a domination by technical forms of expertise; the second is that, in practice, the way biotechnologies actually emerge is less amenable to such disciplining in any case. In particular, the idea that technical questions can be separated from political questions, and these from social and ethical questions, and that each can be dealt with independently is, we will argue, difficult and potentially misleading to apply in practice.

Conclusion

1.34 In this first Chapter, we have drawn attention to the possibility of ambivalence about biotechnology and some of the vicissitudes of its relatively short history. We have suggested that, at both a local and global level, societies are implicitly committed to securing further advances in biotechnology (the 'biotechnology wager'), either through substantial investment of resources that have significant opportunity costs or, more radically, through the urgent need to mitigate present patterns of growth and consumption in order to avoid catastrophic threats to their welfare. We then suggested that commitments to biotechnology are seldom adequately considered in relation to questions of social opportunity cost but that considering them in this way is a helpful approach to understanding their *social value*. We suggest that the segregation, arrogation and sequencing of biotechnology governance contribute to path dependency that makes balanced governance difficult.

1.35 Our intention in this Report is to draw lessons from the introduction (or obstruction) of previous technologies – both biotechnologies and other forms of technology – in order to suggest an ethically robust approach to governance of biotechnologies that are currently being researched, such as synthetic biology, and others that may follow in the future. Our focus will be on how control is exercised over the shaping of research, development and innovation in biotechnologies, and the assumptions and values implied in this. If we are committed to a future in which biotechnologies play a significant part, how this control is exercised matters greatly. It cannot, however, be exercised through crude choices between different ready-made technologies; rather, it concerns the multiple determinations, by numerous actors in multiple contexts, of the conditions that direct, encourage, facilitate, restrict, limit and control biotechnology research, development and innovation. The conditions to which these choices relate include institutional design, funding and investment, law and regulation, and economic and commercial conditions, among many other things. More importantly, it is about the way in which these multiple determinations come together to affect the public interest.

[50] For example, this complaint has been levelled against the US National Institutes of Health-Department of Energy Joint Working Group on Ethical, Legal, and Social Issues (established as part of the Human Genome Project in 1989). For the most part, the Group was restricted in its remit to considering the implications of the project and the related science and technology, rather than whether the investment in the project should have been made in the first place. See: Human Genome News (1990) *NIH-DOE joint working group on ethical, legal, and social issues established*, available at: http://www.ornl.gov/sci/techresources/Human_Genome/publicat/hgn/v2n1/05elsi.shtml.