The Economic Dynamics of Modern Biotechnology

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Johan Brink, Maureen McKelvey and Keith Smith

1. INTRODUCTION

This chapter addresses issues related to conceptualizing and measuring modern biotechnology, thereby raising questions of definitions, methodology and data.[1] This chapter argues that behind many of the empirical and comparative issues lie fundamental problems of conceptualization of the empirical phenomena. Addressing these conceptual problems is important for analytical progress, but also for decision-makers in government policy, universities and firms.

Within this context, the chapter has three purposes. The first purpose is to highlight some key issues about the conceptual choices possible in operationalization and the implications thereof. There is a vast number of different terminologies regarding the usage of the concept 'modern biotechnology' as well as different methodologies, indicators and data. Such diversity is neither surprising nor strange – given that the dynamic nature of the underlying object under study by definition introduces inconsistencies. Still, inconsistencies prevent comparisons, and choices must be made.

The second purpose is to introduce a conceptual matrix to structure one way of thinking about how to conceptualize the empirical phenomena. The objective here is to structure concepts in a way that is useful for analytical work. The approach here is based on the idea of distinguishing clearly between two axes of 'product and sector', on the one hand, and of 'knowledge bases', on the other hand.[2] The concept of 'knowledge base' refers to areas of scientific and technological knowledge, including both the knowledge itself as well as its embodiment in techniques and instrumentation. This conceptual matrix follows on from the first purpose, but aims to take a step further in providing a novel and useful structure of interpretation.

The third purpose is to form a common starting-point in terms of the weight given to methodological considerations in this book, given that all

chapters include significant empirical data. Each chapter makes choices about definitions, methodology and data and these choices together influence 'what is seen' and 'what is concluded'. While diversity exists, nevertheless, authors of this book are united by an awareness of the importance of methodological considerations as well as by a common desire to find more appropriate ways of understanding the empirical phenomena.

Although these issues may appear to be mundane on the surface, dissonance between different definitions and different measurements of the empirical phenomena form the second paradox introduced in Chapter 1. The general problem is that modern biotechnology is an emerging, generic technological area, containing many broad (and internally differentiated) knowledge bases. How then to capture it, without either capturing only irrelevant details or missing the main point?

This chapter begins by comparing and contrasting definitions in Section 2. A conceptual matrix for understanding modern biotechnology is then proposed in Section 3, based on the two axes of 'product (sector)' and 'knowledge base'. Section 4 raises some central issues related to the operationalization of this concept through data and statistics. This chapter does not purport to offer a universal solution – instead, the purpose is to raise awareness of the choices (and implications thereof) of definitions, methodology and data for analysing the empirical phenomena.

2. DEFINING MODERN BIOTECHNOLOGY – AND RELATED CONCEPTS

While Chapter 1 gave a quick insight in the context of this book, this section compares definitions of modern biotechnology and related concepts in more detail. This is done partly in order to provide a broad framework for the book and partly in order to be able to discuss operationalization of concepts in the subsequent sections.

Roughly speaking, biotechnology is defined as the application of knowledge of living organisms and their components, to industrial products and processes. It has already been claimed that a diversity of definitions exists – and even more so for operationalization. Some studies focus almost exclusively on a particular industry or type of firms, whereas others claim that modern biotechnology should by now be widely regarded as a diverse set of knowledge bases and an enabling technology, rather than as a distinct industry or sector *per se*. Clearly, the knowledge, techniques and tools of modern biotechnology have diffused and affected quite different application areas and industries. Examples of areas affected include human health care, drug development and pharmaceuticals, food production and

processing, new materials and fine chemicals, energy, sensors and such environmental applications as bioremediation.

Many different definitions exist in the literature, ranging from reports published by internationally influential bodies such as the Organisation for Economic Co-operation and Development (OECD), through government agencies and consultancies to studies undertaken by academic researchers in the social sciences. A list of definitions follows, containing examples from government reports, industry associations and the social sciences. While the OECD definition is currently among the most frequently cited, the point here is that many other definitions exist as well, and these open up considerable space for diversity in interpretation, measurement and policy ideas.

- The OECD (OECD 2003):'Biotechnology is the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services.'
- The Office of Technology Assessment in the USA in 1984 (OTA 1984): 'Modern biotechnology incorporates a specific focus on industrial usage of rDNA, cell fusion and novel bioprocessing techniques. Industrial use of living organisms rDNA: New drugs, food, chemicals, degradation of toxics.'
- The European Federation of Biotechnology (EFB 1982 as referred in OTA 1984): 'Biotechnology is the integration of biochemistry, microbiology and engineering sciences in order to achieve technological (industrial) application of the capabilities of micro-organisms, cultured tissue cells and parts thereof.'
- The Office of Technology Assessment in the USA in 1991 (OTA 1991): OTA introduces the commercial activities around biotechnology as 'a new set of techniques that can be used in basic research, product development, and manufacturing in several different industries'.
- The Lord Sainsbury report in the UK (Sainsbury 1999):[3] 'Biotechnology companies are those whose primary business focus is the commercialization of these new technologies . . . The sectors for which biotechnology holds most promise includes pharmaceuticals, agriculture and food.'
- The Biotechnology Industry Organization in the USA in 2003 (BIO 2003): 'New biotechnology – the use of cellular and molecular processes to solve problems or make products . . . Biotechnologies capitalizing on the attributes of cells and biological molecules.'
- (Powell, et al. 1996): 'In many respects, biotechnology is not an industry *per se*, but a set of technologies with the potential to trans-

form various fields. Many researchers treat the wide array of biotechnology companies as comparable. In contrast, we intentionally restrict our attention to only those for-profit firms engaged principally in human therapeutics and diagnostics, hereafter referred to as dedicated biotechnology firms, DBFs.'

- Zucker and Darby (1997): 'The revolution in the biosciences has transformed technologies used in many other industries (including medical supply, chemical, agricultural, food-processing, and brewing), but none so rapidly and dramatically as in drug discovery'. They further argue that a biotechnology is generally defined more narrowly in terms of using breakthrough technologies such as genetic engineering.
- Feldman and Ronzio (2001): The definition includes combinatorial chemistry and liposomes to fields of chemistry and fermentation, large-scale cell culture and tissue culture.
- Carlsson (2002): Bio-industries transition is due to the new biotechnology and information technologies. Bio-industries is defined as such: 'Fundamentally dependent on the generation, processing or manipulation of biological systems and materials. This includes health care and medical services, agriculture and food technology, environmental technologies, biomaterials, large sectors of chemical technology, parts of the energy sector and several others.' The study includes biomedicine more generally, medical devices, instruments and supplies as well as applications outside the health care sector such as food, agriculture and forestry.

The OECD definition is widely used but is quite narrowly delineated in relation to a techno-economic context. One problem with the OECD definition is that the convergence of modern biotech research with other fields implies that it is becoming increasingly difficult – and perhaps meaningless – to distinguish traditional chemical and medical research from those dependent on modern biotechnology. Therefore, the OECD is currently reworking their biotech definition to improve the ability to characterize different forms of biotechnology, based on the five areas of knowledge listed in Chapter 1. Looking at other definitions, one can see a strong variety in terms of concentration on the fields of application, types of companies and economic sectors as well as in terms of the underlying knowledge and technologies.

Problems of definition feed directly into problems in the development of international statistics to capture the phenomena of modern biotechnology. Some of these challenges are similar to the earlier challenges in understanding information technology (IT) and informtion and communication

technologies (ICT) industries within modern society. Here, one problem was an often sharp dichotomy between the small size of manufacturing ICT sectors, and the large claims made for the economic impacts of IT in terms of productivity impacts in other industries. Statistical agencies coordinated through the OECD responded to this challenge by expanding the scope of what was regarded as ICT industries. Similar problems arise with respect to modern biotechnology. Thus, the attempts by national statistics agencies and the OECD to harmonize definitions and statistics are quite important in a longer-term perspective of analysing the phenomena.

One way to help sort out the difficulties of giving the 'right' definition is to understand that modern biotechnology is part of a knowledge frontier, with a past, a present and a future (see Chapter 3). Modern biotechnology is more than the current scientific discoveries and current products in the market. It also includes a past trajectory of development of knowledge, techniques and tools – and where all the accumulated knowledge is included. It includes a current 'state of the art' and in the future, new discoveries and interpretations will change what we understand and what we can do. The historical processes matter, and thereby draw our attention to the span of relevant knowledge, techniques and instrumentation. The earlier generations of biotechnology have also continuously co-evolved with 'modern' ones, since the process of knowledge generation is both cumulative and self-reinforced. This also means, moreover, that the knowledge base and its evolution make borders between sub-fields blurred and intertwined over time.

The 'modern' in modern biotechnology is often used as a way to differentiate the present from the past. First generation, or traditional, biotechnology has been a part of human history ever since the early usage of yeast and bacteria for food processing, and selective animal breeding for desired traits. In the early twentieth century, the second generation of biotechnology became a tool in the hands of engineers when biologically based production processes became industrialized. Examples of first- and second-generation biotechnology include the usage of biological-based mechanisms in food processing; alcohol and diary production; and bioprocessing in order to make biopharmaceuticals and fine chemicals, such as penicillin and citric acid respectively. The age of modern, or third generation, biotechnology is dated back to the discovery of the DNA molecule by Watson and Crick in 1953. Their discovery – that is, their solving of the scientific puzzle in understanding DNA – became the starting point of a new era. The third generation is explicitly based on underlying scientific progress whereas the first and second generation were more technological applications, without a solid scientific understanding of the underlying biological processes.[4]

Not even 'modern biotechnology' can be taken for granted, however, as a definition set in stone. Modern biotechnology depends on advances in many fields of medical science, natural science and engineering. During the latest 30 years, the scientific and technological knowledge about biological mechanisms has grown tremendously. Modern biotechnology is more than knowledge – indeed its impacts come about through the combination of increasing knowledge with techniques and instrumentation. Two generic techniques have been particularly influential in terms of enabling the diffusion of biotechnology into new areas, namely the recombinant DNA technique by Boyer and Cohen in 1973 and the monoclonal antibody or hybridoma technology by Milstein and Kohler's discovery in 1975. These two techniques rapidly found industrial applications, for example, in diagnostics and in biopharmaceuticals like insulin and human growth hormone made from genetically modified bacteria (or yeast). More recently, the sequencing of the human genome and the genomes of several other organisms has been more or less fully completed. This systematic genetic information and related IT tools are claimed to represent a milestone, and in this post-genomic era (PGE), an increasing number of scientists around the world are engaged in the study of the function of genes and the proteins they are coding for. Thus, proteomics and metabolomics have become expanding research fields that contribute to enhance our understanding of, and ability to modify, life processes. The merging of modern biotechnology with other areas like IT has also led to new fields, such as DNA chips and bioinformatics.

Such developments matter for industrial applications in specific settings. They have fundamentally changed the drug development process in pharmacueticals (Nightingale 2000). In doing so, it has enhanced the efficiency and effectiveness of the research and development (R&D) process, especially related to finding and testing potential target molecules and candidate drugs. Hence, the R&D process is changed also for new drugs that are manufactured by more conventional means (e.g. organic chemical synthesis).

Multiple definitions and confusion about terminology is not surprising – given this highly dynamic process, where both knowledge and applications are continuously being developed. However, the lack of a clear definition is unfortunate, because not having one means it is difficult to conduct stringent analysis and to compare and contrast cases. This situation is likely compounded by the fact that analysts have different backgrounds – and the importance of diverse backgrounds may be obvious if we consider that analysts includes natural scientists, medical researchers, firm managers, government policy-makers, journalists, management consultants, social scientists (including economists) and so on.[5] This suggests that neither

shared worldview nor generally accepted terminology exists, and hence definitions and statements must be critically examined with great care.[6]

Thus, when moving from these broad official definitions to actual studies and the interpretation of results, it is clear that the broad definition and understanding has to be turned into criteria, which can be used to categorize a process, event or outcome as modern biotechnology. This holds in general as well as for each chapter within this book. Such criteria matter because, at this point, the decisions about what to actually include – or exclude – will have a large impact on many follow-on issues. It can affect how many firms are counted; the relative specialization into sub-sectors; the type, quantity and quality of science assessed; which industries are understood as affected by modern biotechnology and so on.

3. A CONCEPTUAL MATRIX FOR MODERN BIOTECHNOLOGY

This section presents a conceptual matrix, aimed at outlining the essential dimensions of modern biotechnology, along the two axes of 'product (sector)' and 'knowledge base'. It proceeds by discussing possible definitions, methodology and data for each axis in turn. These two axes then intersect to provide the conceptual matrix. The suggestion is that the conceptual matrix ought to be useful to clarify the lines of debate and to nuance the interpretation of research results, both of this book and in future research.

The first axis is that of the product-based (sector) one. The discussion first addresses how the definition of similar products or product groups is usually used to identify an industrial sector. From there, the discussion applies this axis to modern biotechnology, based on reasoning about the relationship between 'core' biotechnology and associated sectors.

The product-based (sector) axis requires the concept of an industry, with roots in economics and industrial organization. Such a definition starts from the firm's ability to supply specific products (used in certain ways) and from that, classifies each firm into a certain industry. This type of economic reasoning is traditionally linked to governmental data and statistics, and the Standard Industrial Classification system (SIC) from the US Bureau of the Census is the most commonly used way to classify firms and industries for statistical data.[7] Once the industrial sectors are set, categories and comparisons can be made across industries, based on characteristics of the production process.

A different way to proceed to define an industry could be based on characteristics of the 'market' on the demand side. For example (Payson 2000)

argues that a function-based definition of classes of products is suitable as a complement to the traditional product and industry definitions. In other words, in his argument, the function of a product relative to the needs of the user would allow us to group sets of apparently different products (industries) based on 'use'. If the demand side were further emphasized, then 'markets' could further be defined from a customer perspective, using product characteristics and functions (Lancaster 1966), and could specify certain geographical considerations. The human health care sector as related to modern biotechnology would fit this perspective, that is the aggregated biomedical industry including medical technology, instruments and medical supplies fulfilling the various health care demands (Laage-Hellman 1998). However, this way of defining markets should be most suitable for tangible products. By focusing only on product characteristics and functions, the definition is also difficult to implement in practice.

A comprehensive definition of a product (sector) could be based on a combination of supply and demand sides, thus including the competing product, characteristics of production knowledge and the specific demands of users. A relevant example could be those biopharmaceuticals, which are supplied with the help of modern biotechnology and fulfil the need for therapeutics in human health care.

As discussed further in the next section, trade data refers to a group that is almost entirely based on biologics. This definition both includes many products that are not part of modern biotechnology and excludes other important products based on biotechnology.

Moreover, in national surveys as well as in specific studies, the concept of dedicated biotech firms (DBF) is often erroneously identified as the biotech industries *per se*. DBFs can be delimited in a number of ways, based either on the product, production knowledge and/or use. Delimitations can be set to products towards therapeutics and diagnostics for human needs (Powell et al. 1996) or more widely to modern biotechnology as used in all possible product groups (OECD 2001). A reason for capturing not only these small, start-up firms is that the DBFs are in fact often developing products in both cooperation and competition with firms in existing industries (OTA 1991). (See also Chapter 3.)

The proposal here is that the product-based (sector) axis should include both 'core' biotech as well as associated sectors, as illustrated in Figure 2.1.

Figure 2.1 provides a means of identifying and distinguishing the products (sector) of 'core' biotechnology from the use and intersection of biotechnology with various industrial sectors such as pharmaceuticals, food and medical technology. As argued in McKelvey (forthcoming) and in Chapter 10 of this book, linking products (sectors) based on the core knowledge to various existing sectors matters in terms of results.

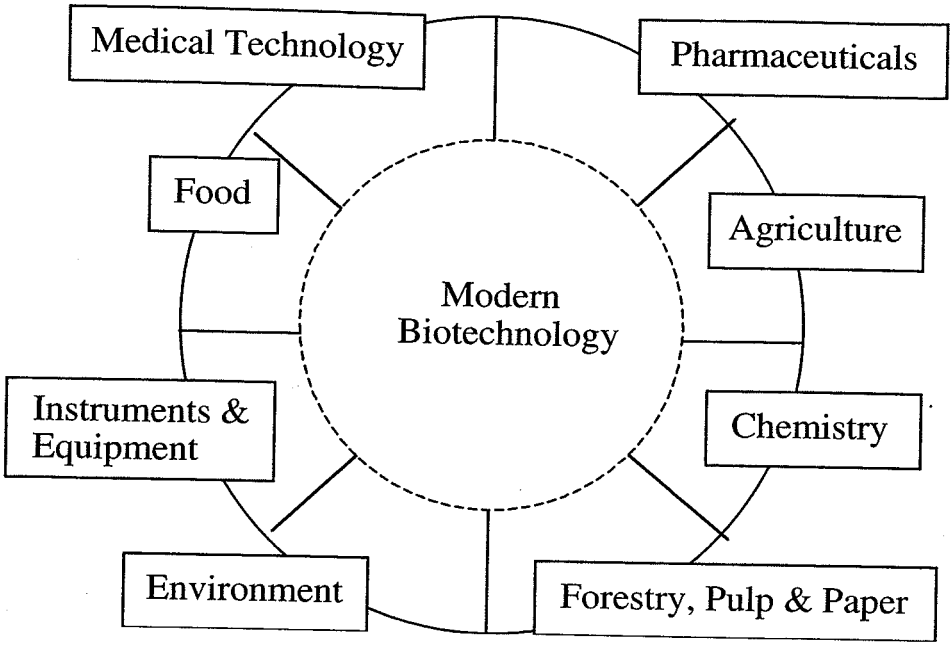

Figure 2.1 *Axis of product-based (sectors) in biotechnology: A combination of 'core biotechnology' and sectors*

In this way, Figure 2.1 can capture elements found in the broad definition of modern biotechnology, such as the OECD definition. This way of defining modern biotechnology from the product (sector) thereby forms one of the two axes in the conceptual matrix.

The second axis is formed by the knowledge bases. This discussion briefly presents the arguments, then mainly addresses the special case of modern biotechnology.

The argument for this axis arises from the conceptualization that knowledge bases – including knowledge, techniques and tools organized by various ways such as disciplines – affect the economic uses and impacts of science and technology. For emerging technological areas, it is rather common to begin with a list of relevant fields. The problems, however, often arise when such a list is applied to a purpose. It may be difficult to compile as well as to maintain, once the dynamic aspect is considered. A list may be difficult to use, once industrial applications are considered since they usually require a variety of fields and interdisciplinarity for problem-solving. This often requires classification based on knowledge bases, thereby leading to problems of classification of firms and/or products.

In general, one problem of only using knowledge bases to define an area like modern biotechnology is that at any time, a long list could be made. It should include all relevant scientific and technological fields of knowledge, techniques and tools, as has been exemplified previously. For example,

Chapter 1 presented the five areas that the OECD *ad hoc* group is considering using to define the boundaries of modern biotechnology.

Hence, a related complication is the growth and increasing scope of relevant knowledge bases. Even a well-defined and unambiguous list of relevant knowledge will be outdated as further developments occur in the future.

Another problem is that any one product or firm will often use a variety of knowledge bases. While multiple knowledge bases are an inherent fact of economic life for firms, this presents some problems of categorization when used in order to categorize actual firms into product (sector) classifications.

A related observation is that biotech knowledge bases often have many general areas of applications, which cut across traditional industries. This leads to some measurement difficulties due to heterogeneity of activities.[8] Such a diversity of firms to be classified implies a methodological problem. Should only new biotech firms be considered or should firms diversifying into biotechnology be included? If diversified firms are included, is it the fraction specialized into biotechnology that is interesting or is it the whole firm (Swann and Prevezer 1996), due to its access to existing complementary resources?

The generic nature of many knowledge bases relevant to modern biotechnology implies that the companies involved can be found in different business sectors. More than that, it implies that these firms and sectors are to a varying degree specialized in biotech-related applications. Some may mostly be focused around biotech knowledge whereas others use it as input into research, production processes and/or products. As with the first axis of product (sector), this second axis of knowledge base is useful for certain purposes. It helps identify a changing list of relevant knowledge, techniques and tools at any given period and to identify their spread and impacts across a variety of other sectors over time.

The conceptual matrix proposed here is a combination of the product (industrial sector) axis and the knowledge axis. The combination should provide advantages as compared to using only one or the other approach, and thereby be useful for conceptualizing and measuring modern biotechnology. The conceptual matrix is based on the two axes, which provide classifications based both on product (industrial sector) as well as on knowledge.

Figure 2.2 illustrates the conceptual matrix, followed by examples relevant to modern biotechnology.

The conceptual framework in Figure 2.2 should be useful in order to identify and group together various definitions, methods and data, and thereby also to interpret results and design new studies.

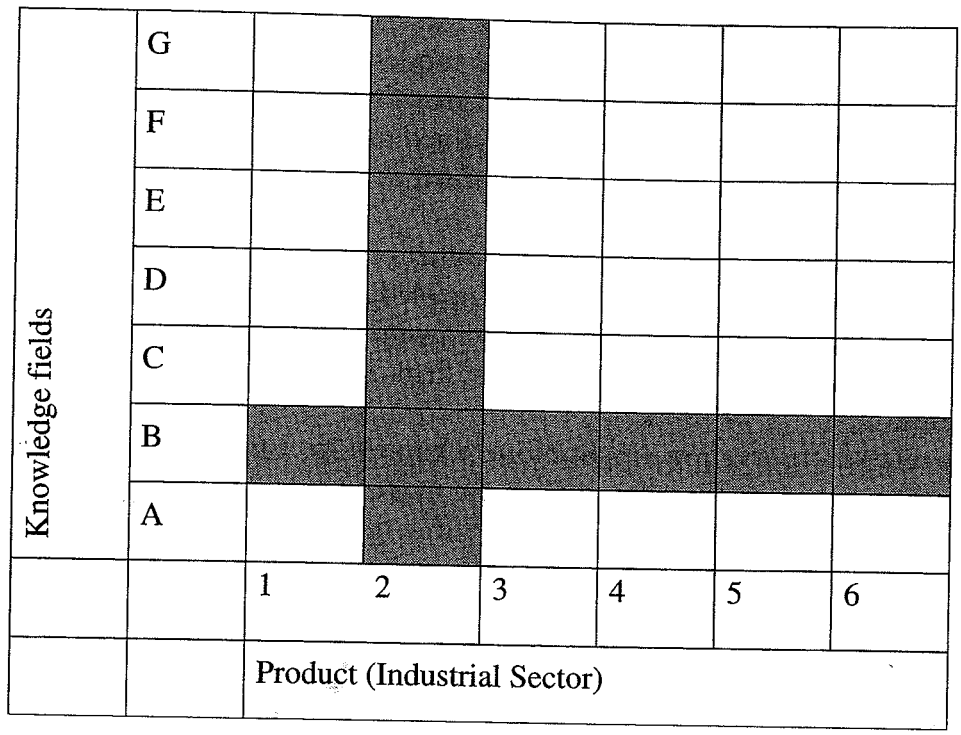

Figure 2.2 Conceptual matrix based on the two axes

Turning to the first axis of Figure 2.2, the classification into product (industrial sector) implies a focus on products, production technologies and uses. The example can be drawn from the two most obvious product groups or industrial sectors under development today, namely biologics and pharmaceuticals. Both include mainly products to meet human health care needs but the companies also sell somewhat different product and rely on somewhat different production technologies and usage. The axis of 'knowledge' can be used to define fields and/or more general concepts. Examples of fields would include specific disciplines like bioinformatics or molecular biology. Example of more general concepts could be life science (bioscience).

The conceptual matrix becomes interesting, when a combination of product (sector) and of knowledge bases are used to further specify the phenomena studied. Take the first example of biologics and pharmaceuticals as products (sectors). While both product classes involve the development and use of modern biotechnology in the research process, the firms making them also rely on many other areas of knowledge. Most pharmaceuticals are mainly produced with traditional chemistry, not least as producing pharmaceuticals based on genetically modified organisms (GMOs) proved costly and/or impossible for certain categories of drugs. Similar arguments can be made for medical technology, biotech devices, agriculture

and environmental engineering. They face certain market conditions, but also rely on both generic and more specific biotech knowledge bases.

One way to allow for both precision and shifting boundaries is to include both the product (industry) axis and the knowledge axis within the same conceptual matrix. This is one way to allow for both rigidity and plasticity, given that a precise and complete definition of modern biotechnology will never occur since the field of modern biotechnology is highly dynamic. New products and applications will be introduced and intermediary products and biotechnology-based production processes will diffuse to quite different industries[9] – thereby affecting their products as well as their productivity and profitability.[10] New technologies and applications will continuously rupture agreement over classification into product and sector (industry).

4. METHODOLOGY AND DATA

At present, there are serious difficulties in gauging the overall dimensions and dynamics of modern biotechnology within the economic system, mainly because of limitations in available indicators and statistics. This section discusses some crucial conceptual and practical problems of moving from a concept (definition) to operationalization. Any attempt to grasp modern biotechnology faces these problems, and the discussion first takes it from the viewpoint of economic statistics, then looks at available data and what they tell us, and finally discusses economic indicators of biotechnology.

The basic difficulty with quantitative approaches lies precisely in the fact that this is not a sector but a technological area (see Chapter 3). Moreover, modern biotechnology has many product dimensions, different underlying knowledge bases and wide fields of application. These complex product and sector aspects of biotechnology preclude any straightforward economic measurement. This is important, since although biotechnology is an emerging technology, it is one for which significant economic claims are being made. So although this section discusses all areas of biotech data, the focus is on areas of actual or potential economic measurement, especially in fields where existing data limitations might be overcome.

The main data sources for biotechnology activities or products at the present include:

- trade data classified by product group;
- specialized surveys of firms engaged in some form of biotechnology production, in terms of output, employment, alliances and so on;

- surveys of 'technology use' at firm level;
- scientific publications' data;
- patent data, either United States Patent and Trademark Office (USPTO) or European Patent Office (EPO);
- R&D data covering expenditure and personnel, classified by socio-economic objectives and fields of research;
- databases on specific topics, such as alliances, venture capital, firms and so on.

Before turning to these specific types of data, some general comments. One immediate need is for agreed cross-country definitions to use for statistical purposes. This should encompass not only agreement about what constitutes a biotech process, but should also relate to biotechnology activities such that it is possible to distinguish between sectors on the basis of their dependence or incorporation of these activities. Such a definition could then be used in relation to more than one data source.

Such a common approach does not exist mainly because national statistics offices do not always collect biotechnology data, and there is little coodination between the organizations who do collect. These collecting organizations also have quite different motivations and objectives. Within the OECD countries, data are currently collected by a disparate group of agencies – statistical offices, consulting companies (particularly Ernst & Young), business associations, regulatory agencies, industry ministries, universities and research-funding organizations. Only four countries (Canada, Italy, The Netherlands and New Zealand) carry out industry surveys through their national statistical offices. Data for at least four countries comes from consulting companies, for three from industry associations and for another four from ministries or R&D funding agencies. As we might expect, definition and collection methodologies differ sharply, often reflecting the specialized interests of whoever is collecting the data. So some data collectors may be interested in new firm creation, and some may be interested in R&D performance. In Norway, for example, data collection is in the hands of the agency that regulates genetically modified organisms. These different interests of course shape sample selection and hence statistical coverage. In addition, of course, specific studies may rely on their own selection and sample of data, which they have collected themselves, but that data is only sometimes available publicly.

Turning to specific types of data, trade data classified by product groups, and this obviously requires a standardized definition before this type of data can be collected. One way out of this dilemma for trade statistics has been to focus only on a subset of biotechnology. As there is no real disagreement on one area, namely biotechnology based on recombinant

DNA, some sources confine themselves to this only. However, this tends in practice to lead to a focus on biologics, namely therapeutic products derived from living organisms, and this is used in trade statistics. This emphasis excludes, for example, 'traditional' biotech processes, particularly in food products. But this definition also excludes such emerging areas as plant or agricultural biotechnology, and environmental biotechnology. So, one result of focusing on biologics in trade data is that biotechnology trade is extremely small (about 1 per cent of US product trade) and very limited in geographical focus (most of it goes to a limited group of countries).

The second and third types of data require surveys of firms, and many countries have carried out surveys of firms engaged in some dimension of modern biotechnology.[11] Most of these surveys consist of counts of companies, of R&D within them, of sales and sales growth and of personnel. In some cases there are venture capital data related to seed stage funding committed to biotechnology companies. Similar studies may be carried out by individual researchers, but the discussion here mainly focuses on more public data, carried out by official sources and/or used for government purposes.

These surveys are far from comparable internationally. The best survey is OECD (2001). The basic problems start with firm definitions, that is the problem of defining a biotech company. Furthermore, some data gatherers report data on biotech companies without ever reporting their definitions or selection criteria, and this of course suggests a strong probability of biases in coverage. Many seem to rely on a definition of 'core biotech' firms that rests on whether firms are using some form of recombinant DNA technology. In Australia, the definition of a biotech firm is one that 'is entirely or substantially biotechnology related and that has a significant commitment to technological innovation' (OECD 2001). Canada uses a similar definition, but adds all firms that perform any biotechnology R&D. Germany uses a similar definition of core companies, but classifies them as 'entrepreneurial' or not, and adds 'extended' companies that are not purely in life sciences. The picture that emerges focuses heavily on firms involved in pharmaceuticals and health care applications.

The central problem with these definitions of 'core' biotech firms is that they sharply constrain what is counted as modern biotechnology. In those countries that look more specifically for the application of biotechnology methods across industries, a different picture emerges. Italy has no definition of biotech research but collects data by asking questions about biotechnology research through its R&D survey. This has the interesting result of showing that eight major sectors perform biotech R&D including motor vehicles and fabricated metal products (the latter is interesting since it is one of the largest industries in Europe). The largest expenditure on biotech

R&D in Italy occurred in the water supply industry. A similar result can be found with Japan, which focuses its survey on biotech activities. This leads to the biggest proportion of 'biotech' firms being located in the food and drink industry, with substantial presence also in metals and machinery industries. Presumably these results reflect the multi-technology nature of modern firms, but in any event the results are sharply different from those in countries that focus on 'core' biotech start-ups.

Similar results emerge from Canada, which has shifted away from gathering data based on the notion of 'core biotech firms' to one based on 'innovative biotechnology firms. The latter means a firm that 'uses biotechnology for the purpose of developing new products and is engaged in biotechnology related R&D' (McNiven et al. 2003). This definition enables Statistics Canada to extend into different forms of biotechnology, and to extend the sectoral scope of the investigation, covering health, agriculture, natural resources, environment, aquaculture, bioinformatics and food processing. Part of the reason for this redefinition is that previous surveys had shown considerably more firms using biotechnology outside the 'core' biotech definition than inside it – 358 core biotech firms, but 784 user firms in 1996 (McNiven 2002). Health is certainly the largest revenue-earning sector from biotech products (generating 71 per cent of all biotech revenues in Canada) but all sectors mentioned above are generating revenues from innovative products, particularly food processing, environment and agriculture.

So the point that emerges here is that restricted definitions of biotech firms not only limit the scope for international comparability, but they can also present a quite misleading picture of the extent of biotech research and production. Where countries such as Australia focus on a core biotech sector and exclude 'traditional' biotechnology or more importantly agricultural biotechnology, then a quite distorted pattern emerges.

A fourth type of data is scientific publications. A central feature of modern biotechnology is its close connection with the relevant science base, and its close organizational connection to universities. This means that bibliometric data, emerging from analyses of scientific publications patterns, is more than usually relevant for understanding innovation patterns. Once again, there are limitations, which are here discussed in terms of publishing strategies and problems concerning journal coverage.

The strategy issue is that publishing requires disclosure, while innovation usually requires limits to disclosure in the interests of appropriability. On the one hand, secrecy is a very basic strategy for innovating firms – often far more important than patenting as an appropriablity measure. On the other hand, firms may have strategic reasons to publish, such as to signal their involvement in a field and gain access to the international research community, attract partners and future employees and so on.

A related difficulty is journal coverage. Most biotech publication data in fact covers predominantly health-related areas – microbiology, oncology and so on. There seem to be persistent problems in defining appropriate biotechnology coverage in agricultural or environmental applications, and this exacerbates the partial picture referred to above. So while bibliometric data is extremely useful in mapping both search patterns and impacts (measured via citations) in areas where publication is an important strategy for firms, it is not a general indicator of the trajectories of change in biotechnology.

A fifth type of data is patents. Within innovation studies, counts of patent applications and granted patents are a major source of quantitative data. A well-known limitation is that there are more or less non-quantifiable variations in the propensity to patent, across firms, industries and countries.

In the case of modern biotechnology there are also classification differences across patent offices. The most important differences are between USPTO and EPO. There are differences between when a patent is acknowledged (in the year of application or year of grant) that affects the data, but more important are sometimes subtle differences in definition. The US definitions begin from a very wide view: 'technologies related to the analysis and application of the genomes of all creatures', while the European definitions relate more strictly to microorganisms and enzymes.[12] Once again, while patent data are immensely useful, they are far from standardized or definitive. Various categories of other patents may be included within a count of biotechnology patents, a choice which affects which types of technologies to include or exclude and thereby the results.

A sixth type of data is R&D surveys, a more recent development. Of course it must always be borne in mind that R&D is only one among many innovation inputs. Despite limitations, R&D surveys are the only data source for biotechnology that are coordinated and indeed standardized (via the OECD's *Frascati Manual*). The problems here lie not so much in data quality as in differences in country collection practices and data availability.

Most R&D data are reported along two dimensions, namely expenditure and personnel. These are normally reported in terms of sources of funding (i.e. business, government, foundations etc.) and sectors of performance (i.e. business, universities, government etc.). Among the advanced economies, the surveys often go far beyond this and have some more or less unique features that permit a detailed understanding of the structure of R&D performance. This is because, as well as collecting data on sources of funding and sectors of performance, the surveys for R&D data also provide four other types of breakdown of R&D expenditure. For the business

sector the data breaks down performance by International Standard Industrial Classification (ISIC) category, that is by the industry which is performing research. For all sectors, there are three further ways of breaking down R&D expenditure and personnel resources. These are:

1. by socio-economic objective (such as economic development, defence, health, environment etc.);
2. by type of research (that is, pure basic research, strategic basic research, applied research or experimental development);
3. by field of research (meaning the specific area in which new knowledge is sought, such as molecular biology, applied mathematics, electronic engineering and so on).

The latter make it possible to gain a detailed picture of how R&D is prioritized towards specific areas of research.

As a concrete example, in Australia the research funding of the private non-profit sector (i.e. charitable foundations) is overwhelmingly directed at one socio-economic objective, namely health. Within this objective, we can look at fields of research – the two largest are clinical medicine and biological sciences. It is then possible to look in detail at the specific research fields that characterize biological sciences. These turn out to be genetic, cell biology and biotechnology. Turning to the disaggregated data we can then identify specific priority areas, as in Table 2.1.

Table 2.1 suggests that national statistics can be used to identify rather specific investments in different fields within – or related to – modern bio-

Table 2.1 Expenditure on Australian private non-profit R&D by research field biological sciences, rank of top 10 performers, 2000–01

Research field – biological sciences	$'000
Gene expression	12331
Cell development (incl. cell division and apoptosis)	8541
Genome structure	8352
Genetic engineering and enzyme technology	4915
Protein targeting and signal transduction	4116
Infectious agents	3293
Gene therapy	3210
Cellular interactions (incl. adhesion, matrix, cell wall)	3129
Genetics not elsewhere classified	3126
Neurogenetics	2940

Source: Australian Bureau of Statistics, R&D statistics.

technology. It is also possible to cross-classify such data by type of research – most of this turns out to be 'strategic basic' research – fundamental research but with application areas in mind.

R&D data exploration of this kind can be extended into business R&D, government-funded R&D, and so on, and thus offers a rather comprehensive picture of a country's overall research effort. It is one of the best ways to identify the complex overall pattern of biotech development in ways that are comparable internationally.

A seventh type of data is collected in databases, which address a specific topic like alliances, venture capital investments, firms and so on. These databases may be public, commercial and/or developed for specific research studies. Examples of alliance databases include ones held by MERIT/CATI, Recombinant Capital and PharmaDeal. An example of a venture capital database include statistics from the European Private Equity and Venture Capital Association (EVCA). An example of firm databases is the BioSweden database on Swedish biotech-pharmaceutical firms (McKelvey et al. 2003). The firm databases of total populations are often compiled, using a variety of public and private sources, including databases, firm surveys, public data on firms, reports to national accounting offices and so on. Other databases may be built as comprehensively as possible, based on a combination of public, commercial and private databases. Each has advantages and disadvantages in terms of coverage, scope and time, but offer at least some possibilities for quantitative studies. Still, important choices must be made, in terms of whether to use public or commercial databases – or invest in a new, privately held database – as well as in terms of the biases introduced by a particular sample included in a database.

In summary, crucial issues about methodology and data must be considered. There is a range of other biotechnology data available – on international trade in biotechnology products, on inter-firm alliances in biotechnology, on firm creation and so on. However all of this data, without exception, suffers from the limitations outlined above. There are serious problems of definition, sampling strategies and coverage that preclude any quantitative generalizations about modern biotechnology either as a technology or as an economic activity, at the present time. Hence, whether public data is used – or whether unique data is developed in an individual study – choices about operationalization need to be carefully considered.

In conclusion, this chapter has sought to discuss the choices possible in the operationalization of the biotechnology concept; to introduce a conceptual matrix; and to form a common starting-point about definitions, methodology and data for the book as a whole. A central concern of social science research is the validity of empirical studies and comparisons for

both theoretical explanations and recommendations for government policy and firms. The suggestion here is that despite the current diversity, greater harmony for comparisons as well as progress in finding ways to analyse new phenomena, is possible.

NOTES

1. This chapter is the second introductory chapter within the book, yet it also initiates the transition to Part III 'Setting the scene'.
2. Sector and industry are used as interchangeable concepts.
3. Note. This report does not specify the technologies referred to.
4. A further distinction can be made between biotechnology as production technology and biotechnology as a searching technology (Henderson et al. 1999). In this taxonomy the first and second generation will be regarded somewhat nearer production technologies and the third generation as more of a search technology. This taxonomy is however not as straightforward as it first seems and relates to the distinction between product and process innovations.
5. Many fields such as neo-Schumpeterian economics, evolutionary economics, science and technology policy, innovation studies, corporate strategy research and regional development have used the example of modern biotechnology to develop new theory.
6. The variety of definitions used to explain any one concept can be exemplified by the different meanings of the term 'life science'. 'Life science' stands for, at the one extreme, the common underlying scientific base for every biologically related activity and at the other extreme, the short-lived business idea to gather both therapeutic and agricultural applications of modern biotechnology under one roof. During the 1990s several mergers between chemical, agricultural and pharmaceutical firms resulted in large diversified life-science firms, for example AstraZeneca, Aventis, DuPont, Monsanto and Novartis.
7. The SIC is from 1997 and was replaced by the North American Industry Classification System (NAICS) but the structure is not drastically different.
8. One solution to this problem would be to deliberately focus even more deeply into specific applications such as one part of diagnostics or for drug delivery and so on. While useful for some purposes, only using such a definition would mean that the more generic nature of the technology would be lost in the details.
9. New non-biotech-based but highly intertwined knowledge areas are exemplified by; bioinformatics, an information technology for biotech applications and biomaterials, through new biotech-based research methods and materials in the emergence of tissue engineering.
10. During the 1970s a strictly genetic view dominated and modern biotechnology was defined by genetic engineering and hybridoma technologies only. This eventually led to a problem since other aspects of biotechnology continuously were coevolving. A present example is the case of tissue engineering, which has increased the interest in different aspects of modern cell culturing, a high-tech application of the traditionally bioprocessing technology.
11. OECD (2001), 'Biotechnology statistics in OECD member countries: compendium of existing national statistics', STI working paper 2001/6 presents a comprehensive overview of these surveys.
12. See OECD (2003 op. cit., p. 10) for a detailed analysis.

REFERENCES

Biotechnology Industry Organization (BIO) (2003), website www.bio.org/er/, viewed 30 May 2003.

Carlsson, B. (2002), *Technological Systems in the Bio Industries: An International Study*, Boston and Dordrecht: Kluwer Academic Publishers.

Feldman, M.P. and C. Ronzio (2001), 'Closing the innovative loop: moving from the laboratory to the shop floor in biotechnology manufacturing', *Entrepreneurship & Regional Development* **13**, 1–16.

Henderson, R., L. Orsenigo and G. Pisano (1999), 'The pharmaceutical industry and the revolution in molecular biology: exploring the interactions between scientific, institutional and organizational change', in D.N. Mowery and R. Cambridge (eds), *The Sources of Industrial Advantages*, Cambridge: Cambridge University Press.

Laage-Hellman, J. (1998), *Den biomedicinska industrin i Sverige*, Stockholm: NUTEK.

Lancaster, K. (1966). 'A new approach to consumer theory', *Journal of Political Economy* **74**(2), 132–57.

McKelvey, M. (forthcoming), 'Biotechnology industries', in H. Horst and A. Pyka (eds), *Companion on Neo-Schumpeterian Economics*, Cheltenham UK and Northampton, USA: Edward Elgar.

McKelvey, M., H. Alm and M. Riccaboni (2003), 'Does co-location matter for formal knowledge collaboration in the Swedish biotechnology-pharmaceutical sector?', *Research Policy*, **32**, 483–501.

McNiven, C. (2002), 'Use of biotechnologies in the Canadian industrial sector: results from the biotechnology use and development survey – 1999', Statistics Canada working paper, March.

McNiven, C., L. Raoub and N. Traoré (2003), 'Features of Canadian biotechnology innovative firms: results from the biotechnology use and development survey – 2001', Statistics Canada working paper, March.

Nightingale, P. (2000), 'Economies of scale in experimentation: knowledge and technology in pharmaceutical R&D', *Industrial and Corporate Change*, **9**(2), 315–59.

OECD (Organisation for Economic Co-operation and Development) (2001), *Biotechnology Statistics in OECD Member Countries: Compendium of Existing National Statistics*, Paris: OECD.

OECD (2002), *Frascati Manual*, Paris: OECD.

OECD (2003), 'Statistical definition of biotechnology', website www.oecd.org/EN/document/0,,EN-document-617-1-no-21-31006-617,00.html, viewed 20 May 2003.

OTA (Office of Technology Assessment) (1984), *Commercial Biotechnology: An International Analysis*, Washington, DC: US Congress.

OTA (1991), *Biotechnology in a Global Economy*, Washington, DC: US Congress.

Payson, S. (2000), *Economics, Science and Technology*, Cheltenham, UK and Northampton, MA, USA, Edward Elgar.

Powell, W.W., K.W. Koput and L. Smith-Doerr (1996), 'Interorganizational collaboration and the locus of innovation: networks of learning in biotechnology, *Administrative Science Quarterly*, **41**(1), 116–45.

Sainsbury, Lord (1999), *Biotechnology clusters*, London: Office of Science and Technology.

Swann, P. and M. Prevezer (1996), 'A comparison of the dynamics of industrial clustering in computing and biotechnology', *Research Policy*, **25**, 1139–57.
Zucker, L. and M. Darby (1997), 'Present at the biotechnological revolution: transformation of technological identity for a large incumbent pharmaceutical firm', *Research Policy*, **26**, 429–46.