Exploring interactivity in biomedical innovation: a framework and case study analysis

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Abstract

The literature increasingly recognizes the interactive nature of innovation processes. Biomedical innovation, in particular, tends to be highly interactive. Given the ubiquitous nature of interactivity in biomedical innovation, we argue that the concept of innovation being interactive or distributed is not sufficiently differentiated to capture variation in the management and organization of innovation in the biomedical domain. In this paper, therefore we propose a framework that begins to unpack the interactive nature of innovation processes. This framework has two dimensions, organizational and knowledge integration, which represent, respectively, the mode of managing and organizing inter-firm relationships, and the level of inter-group knowledge combination required. The framework also recognizes the importance of the institutional context in shaping innovation processes. We test our framework with case data from an ongoing study of biomedical innovation in the UK and US.

Keywords: interactive innovation, biomedical innovation, networks, comparative case studies.

Suggested Track: Knowledge creation and innovation, e.g., in R & D

Introduction

The need for innovation – defined as the successful creation of new products, services or processes – is high in all industries but especially in the biomedical area, where breakthroughs in science have the potential to cure or alleviate the symptoms

of diseases that are currently untreatable. However, in areas of emerging technology such as the biomedical field, this exploitation of scientific knowledge is often problematic. For example, the 'biotechnology revolution', promised by decoding the human genetic blueprint, has been reported as failing to materialise (Martin and Nightingale, 2004). Moreover, there are numerous 'breakthroughs' in scientific and technological knowledge that could drastically change medical practice. However, even where safety and effectiveness is validated (e.g. through clinical trials), many such breakthroughs fail to be adopted by medical practitioners (Hilton et al, 2002). Often this is because they do not align well with existing, highly institutionalised, professional and medical practices (Christensen et al, 2000). This means that the exploitation of scientific knowledge may require radical shifts in practices and relationships among diverse stakeholder groups (e.g. different medical professionals, industrial scientists, academic scientists, managers, etc.). In some cases, entrenched power relationships make such shifts impossible (Hilton et al., 2002). This indicates that all (or nearly all) biomedical innovation projects can be characterized as 'interactive', at least in the sense that they are highly interdisciplinary and involve the integration of knowledge across scientific, professional and organizational groups. Many projects can also be characterized as 'systemic production networks'- formal inter-organizational units jointly producing a product or service in pursuit of a super-ordinate goal (cf. Alter and Hage, 1993).

The interactive nature of innovation has been discussed previously. For example, Slappendel (1996) differentiates between individualist, structuralist and interactive perspectives on innovation, with the interactive perspective depicting innovation as occurring through the interactions between the practices of individuals and groups and the social contexts in which they are located. Central to this perspective is the idea that, by developing more interactive and collaborative modes of working, for example through the development of networks and joint practices, knowledge that is distributed across social and organizational boundaries can be recombined and integrated in new, often unpredictable, ways to produce new products, services and processes (Rothwell, 1994; Kline and Rosenburg, 1986). While the interactive perspective has been gaining in popularity (cf. Massey et al, 1992; Rothwell, 1994; Coombes et al, 2002), the ubiquitous nature of interactivity in

biomedical innovation, suggests that the concept of innovation being interactive or distributed is not sufficiently differentiated to capture variation in the management and organization of innovation in the biomedical domain. In this paper, therefore we propose a framework that begins to unpack the interactive nature of innovation processes. We focus here on biomedical innovation processes, but argue that the model that we develop is applicable to other domains. This model is derived from the literature and from the first phase of a three-year research project focusing on biomedical innovation. This model is then tested with empirical case data from the second, ongoing phase of this research. We conclude the paper by discussing the theoretical and practical implications of the framework that we have developed.

Interactive Innovation

The concept of interactive innovation fundamentally assumes that innovation is not a linear process from conception, through design, to implementation and diffusion. Instead it is typically an iterative process, where recursivity is the norm and phases/episodes are conflated (Robertson et al., 1996; Clark et al, 1992; McLoughlin, 1999, Kline 1985). Von Hippel (1988), for example, has illustrated that users can play a decisive role across all phases of the innovation process in the scientific instrument sector. Other research has shown how processes of implementation occur in parallel with, rather than following from, processes of diffusion (see, for example, Fleck's 1994 discussion of 'innofusion' in the development of manufacturing technology). By contrast, the traditional R&D linear model creates a false divide between the creation of knowledge by producers in one context and its application by users in another (Newell et al., 2003). While there is agreement regarding this fundamental aspect of interactive innovation, there are other dimensions of interactivity that can be explored which appear to differentiate innovation processes – even those that can be characterized as interactive. These dimensions are discussed below.

1. Interaction between different organizations: Organisational Integration

Powell and Koput (1996) point out that, when the knowledge base of an industry is both complex and expanding, the sources of expertise will be widely dispersed. This means that the locus of innovation will be found in networks of learning, rather than individual firms. No single organization will hold all the knowledge and resources that are needed to achieve breakthroughs in science and then

to translate, develop and market these into new, commercially viable technologies. Such a view is confirmed by a number of studies of the biotechnology, pharmaceutical and medical device industries, which have noted the increasingly networked nature of innovation in the biotechnology industry (Quéré, M. 2004, Orsenigo, Pammolli, & Riccaboni, 2001, Oliver 2001, Marceau 1999, Liebeskind et al. 1996, Shaw 1993).

Thus, in the biomedical domain, a whole range of different types of organizations are involved in innovation processes, including: Public Research Organizations (PROs), regulatory authorities, small and medium-sized dedicated biotechnology firms, venture capital firms, health care providers and large pharmaceutical companies. As Powell (1998: 230) notes in respect of the biomedical field: 'Inside a densely connected field, organizations must adjust to a novel perspective in which it is no longer necessary to have exclusive, proprietary ownership of an asset in order to extract value from it.' As such, interactive innovation will often be associated with the development of new social mechanisms of organization and governance which regulate the collaborative, and sometimes competitive (Alter & Hage, 1993; Elg & Johansson, 1997), relations between different groups and organizations. In the past, the interactions between these different organizations have tended to be ignored by innovation researchers. As Coombs et al. (2003: 1126) note: 'innovation studies has a long tradition of treating the individual firm as the innovating firm, but the limitations of this are increasingly recognized'.

Having said that, it is by no means the case that all innovation in the biomedical area is now pursued in 'virtual', networked organisational arrangements. Rather, networked arrangements, on the one hand, and organisationally integrated arrangements, could be viewed as *alternatives* for the governance of innovation. For instance, as Pisano (1991) points out, even for biotechnology companies, vertical integration is sometimes a viable alternative to engaging in collaboration with external partners and number of biotechnology companies have grown in size sufficiently to be considered now as large firms.

There is therefore likely to be variation across biomedical innovation processes, with regard to how strongly they rely on inter-organisational collaboration or on organisationally integrated activities. We define this dimension as

Organizational Integration, a relational dimension that focuses on the governance, organization and management of the innovation process.

The two extreme poles of Organisational Integration can be defined as 'loosely coupled', on the one hand, and 'tightly coupled', on the other. In the former, innovation activity is pursued within a network of organizations, anchored around a lead organization (often a biotechnology firm) but with a significant amount of the work being conducted in other organizations. Management is decentralized and dependency on central resources is low (Sawhney & Prandelli, 2000). Where formal contracts exist, these focus on mutual obligations and the allocation of future gains (e.g. revenues generated through patents).

In contrast, in organizationally integrated modes, most of the activity is carried out within a focal firm (typically a large biotechnology or pharmaceutical firm), although often some clearly identified parts of the work (e.g. manufacturing, clinical trials) might be outsourced. Management is more hierarchical (often involving matrix management) and there is high dependency on centralized resources.

Our use of the concept of 'Organizational Integration' resonates with but is not identical to the concept of 'relational capability' proposed by Owen-Smith et al (2002) for describing networked processes that link PRO research and firms. Relational capabilities are an attribute of an institutional system and refer to the extent to which an institutional environment enables organisations to collaborate with organisations specialising in different fields (ibid). Our concept of Organisational Integration addresses a similar concern yet refers more directly to the relational aspect of organisational arrangements, rather than to capabilities.

Table 1: Dimensions of interactivity in biomedical innovation

	Organisational integration	
	Loosely coupled	Tightly coupled

Knowledge Integration	Low	Networked-sequential	Integrated-sequential
	High	Networked-complex	Integrated-complex

2. Interaction between different groups: Knowledge Integration

This aspect of interactivity stresses the involvement in the innovation process of different groups, including managers (Lyles & Schwenk, 1992), professionals, scientists (Knorr-Cetina, 1999) and technicians (Orr, 1990) who each have developed distinctive perspectives or worldviews (Dougherty, 1992) which inform their practice and shape their interactions with other groups. The key in relation to interactive innovation is that these different groups are able to integrate their knowledge. This is because innovation relies not simply on the availability of new knowledge, but also on the ability to *integrate* knowledge across an increasingly distributed array of professional groups and organizations (Powell et al, 1996, Owen-Smith et al, 2002). In contrast to 'knowledge sharing' (where groups come to appreciate and share one anothers' perspectives - Grant 1996), knowledge integration emphasises the combination and deployment of knowledge drawn from different domains in order to achieve specific innovation outcomes (e.g. the development of a new product or process). This concept builds on, and extends, Okhuysen and Eisenhardt's (2002) definition of knowledge integration as a process, whereby individuals combine their information to create new knowledge. As Tuomi (2002) puts it, 'innovation is as much about creating new meanings as it is about creating novel artifacts' (18). As such, interactive innovation depends on the creation of new 'communities of practice' (Lave & Wenger, 1991), or 'networks of practice' (van Maanen & Barley, 1984; Constant, 1987).

Unfortunately, most of the work to date that has recognized this need to integrate dispersed knowledge has tended to focus on the structures of networks that

will facilitate this. Networks are viewed as the 'channels' or 'pipelines' through which knowledge is transferred (Owen-Smith & Powell, 2004). These structural accounts thus tend to neglect the agency involved in the formation of networks, their dependence on trust and social capital (Gupta, Sinha, Koradia, & Patel, 2003; Newell and Swan, 2000; Gupta et al, 2003), and their implications for knowledge integration rather than transfer. As Steward and Conway (2000) note; 'Whilst the configuration and membership of a network is important, it is the *process* of networking that releases the 'potential' of the network' (285).

However, we recognise that it is not always the case that a high degree of genuine knowledge integration is required. Often, 'knowledge' can be traded or acquired, as for instance in the case of Intellectual Property Rights (IPR) that can simply be bought or licensed, and do not require any further social intervention or ongoing interaction. For instance, the significant recent growth of University licensing, particularly in the US, indicates that 'packed knowledge' is increasingly exploited by commercial innovators (Narin, Hamilton, & Olivastro 1997, MacMillan & Hamilton 2003). In such scenarios, the generation and exploitation of knowledge throughout the innovation process will follow more of a *sequential* logic than a logic of complex integration.

In light of these considerations, we expect to see variation in the degree of knowledge integration present in biomedical innovation projects. Our concept of *Knowledge Integration* refers to the degree to which distributed knowledge and practice is to be shared and integrated. Thus, whilst all projects require the integration of knowledge across disciplines and/or organizations, we postulate that they differ in terms of the intensity of knowledge sharing between those involved in upstream science (e.g. scientific research) and those involved in downstream application (e.g. clinical practice). In low knowledge integration projects (e.g. the development of a new vaccine, or new weight loss drug), medical need is well established and implications for medical practice are (or are seen to be) relatively easy to forecast. In such cases the requirement to involve end users in product development is lower. In contrast, in high knowledge integration projects (e.g. in tissue engineering), medical need is uncertain and/or contested and the implications for medical practice are complex and difficult to forecast. Therefore significant efforts are made to enlist

clinical practitioners and integrate their expertise into the early design and development of the product or service.

The concept of 'Knowledge Integration' is also similar, but not identical, to the concept of integrative capability proposed by Owen-Smith et al (2002), which they define as the ability of innovators to move back and forth from basic research to development, and thus to facilitate the translation of basic research into innovations (the concept was previously used by Henderson 1994). Our concept of Knowledge Integration would include such recursive links between different stages of the innovation process but is defined more broadly to include the integration of knowledge and expertise across a wider spectrum of actual and potential involves and stakeholders, i.e. scientists, regulators, physicians, patients, etc.

Interaction between structural influences and the actions of individuals

Slappendel (1996) focused on this aspect of interactivity, suggesting a duality, rather than the traditional dualism associated with the relationship between structure and action (Giddens, 1984). From this perspective, innovation is influenced by, and influences, wider institutional environments. Innovation behaviour is both facilitated and constrained by the institutional context. As such, any innovation is shaped by organizational and societal structures and cultures, as well as by individual and group behaviours and attitudes. Similar concepts have also been advanced by students of regional economies, as for instance in the theory of 'innovative milieux' (Camagni, 1995). This aspect of interactivity emphasizes that it is important to adopt a multi-level analysis when exploring any innovation process, since a focus on only one level (e.g., the individual, the organizational, or the institutional) will overlook reciprocal interactions between action and structure. Table 1, below, summarizes the institutional factors reported to be critical in influencing interactive biomedical innovation, together with literature that identifies the importance of these. These elements of the institutional context will need to be taken into account in any framework of interactive innovation.

	Elements	**Indicative References**

Access to Science & Technology	• Technology transfer • University-industry networks	Owen-Smith, Riccaboni, Pammolli, & Powell, 2002; Casper et al., 2001; McMillan & Hamilton, 2003; Lehrer & Asakawa, 2004
Labour Market	• Career pathways and incentives, • Personal mobility, • Professional identities	Zucker & Darby, 1997; Audretsch & Stephan, 1996; Dasgupta & David, 1994
Capital and Finance	• Venture Capital, • In-house R&D funding • Public and third-sector funding	Lockett, Murray and Wright 2002; Tylecote 1999; Manigart et al 2000; Powell, Koput, Bowie, & Smith-Doerr, 2002
Health Care System, Government Policy & Regulation	• Governance of health care • Regulation of drugs and medical devices • Industry-specific government support	Gelijns & Rosenberg, 1994; Moran & Alexander, 1997

In summary, the traditional linear R&D model of innovation highlights the systematic transfer of codified scientific/technological knowledge across a range of hierarchically organized expert groups. Conversely, interactive innovation is seen to span multiple forms of knowledge, including situated learning (Suchman, 1987) as well as more explicit forms, and involves the translation and transformation of knowledge through the heterarchical coordination of a range of groups, organizations and communities. From the literature, we have identified three dimensions of this interactivity. We recognize that these dimensions are not mutually exclusive – the interplay between the broader context and individual action, for example, will be

related to the perceptions and interests of different stakeholders during the innovation process. However, they are qualitatively different: the first stems from an appreciation of the variety of organizational forms and governance structures that can support interactive innovation processes (a dimension we label organizational integration); the second stems from an appreciation of pluralism of perspectives, understandings and interests that need to be integrated to create and exploit breakthrough science (labelled knowledge integration); and the last stems from an appreciation of the importance of context in shaping innovation processes (labelled institutional context). The purpose of the research reported in this paper was to explore biomedical innovation in relation to these three dimensions, in order to develop a more refined framework depicting the characteristics of such innovation. In the next section we describe the method that we have used. This is followed by a section where we outline the framework that was developed on the basis of the first phase of the research. Cases from our second stage of research are then presented, which provide supporting evidence for this framework. We end the paper with a discussion of the theoretical and practical implications of our work to-date.

Method

The research presented in this paper is part of a larger study of biomedical innovation supported by the ESRC and EPSRC. In this paper we present data from two phases of this research. The first phase of the research involved an extensive interview-based survey in the US (N=41) and UK (N=57). Semi-structured interviews were used (primarily face to face), targeting individuals who had experience of working interactively in the development of medical treatment and service delivery in scientific fields where a high requirement for interactive innovation has already been recognized in both business and public policy (including: biotechnology, genomics, genetics and drug abuse treatment and services). Interviewees were evenly distributed across the professional groups (academic, medical, pharmaceutical and biotechnology organizations). Such broad sampling is useful in the early stages of research for improving generalizability (Graziano and Rawlin, 1993). These data were coded and analyzed using NVivo and the results were used to help develop the analytical framework of biomedical innovation presented in the previous sections. This

analytical framework was then used to guide the second, case study, phase of the research.

The second phase of the research involved collecting case study data. The case studies were selected to represent the different types of biomedical innovation that we had identified from the first phase of research. For this phase, a processual case study approach is being used, whereby events are tracked over time (time-series data collection) in an attempt to explain how certain patterns of events located in particular contexts lead to particular outcomes (Pettigrew, 1985). These cases are ongoing and here we report on preliminary data collected at our case sites.

The cases selected are all examples of interactive innovation aimed at producing commercially viable biomedical treatments and services. More specifically, each of the cases represents a project that is aimed at exploiting and developing scientific breakthroughs. In total, we have 11 ongoing case sites in the UK and US. Fifty-two interviews have been completed to date, together with site visits and non-participant observation at relevant meetings. For this paper, we report on four of these cases, selected to exemplify the characteristics of the typology from our framework. We actually have matching cases across the UK and US, but given space limitations we are not going to discuss comparative national cases in this paper. Instead, we simply provide exemplars of the different quadrants of our framework. Data is being collected via semi-structured interviews with key stakeholders in each project, with the recognition that membership may change over time (Wolcott, 1995). The interview protocol has been designed from the data collected in the first phase of this research project.

Given that this process entails a significant degree of inductive research, comparative case analysis has been an iterative process, whereby the data has been constantly revisited, patterns observed, and checked against the understandings of those involved (Yin, 1984, Eisenhardt, 1989). To insure validity, however, qualitative data must be checked against the criteria of credibility and transferability (Denzin and Lincoln, 1998). To aid data credibility, interview data has been initially coded using the coding scheme developed by the research team in Phase 1.

Results

First Phase Exploratory Interviews

Our first phase interviews demonstrated that there was considerable variation between projects in terms of both organizational and knowledge integration – as anticipated by our conceptual model developed above. With respect to organizational integration, projects ranged from networked ('loosely-coupled') modes to organizationally integrated ('tightly coupled') modes. Equally, with respect to knowledge integration, project ranged from highly integrated modes – requiring the synchronous involvement of multiple parties across the innovation process – to less integrated modes.

Institutional Context

		Organisational integration	
		Loosely coupled/ decentred	Tightly coupled/ centred
Knowledge Integration	Low	Diagnostic Labs	AmericanBio PROTEIN
	High	Nowgen	AmericanBio ELBOW

Figure 2: Conceptual framework: Models of Interactive Innovation

Apart from the organizational and knowledge integration dimensions, this framework also highlights that innovation exists within a unique institutional context which will impact the two types of interactions that are depicted. In our own research, we are considering this contextual element of interactivity through a comparative

study of biomedical innovation processes in the UK and the US and have selected cases from each country that fit into the four dimensions arising from our characterization of organizational and knowledge integration. However, as we are not presenting comparative results in this paper; we concentrate on the organizational and knowledge integration dimensions. In the next section, we present four cases from the second, ongoing phase of the research, each illustrating one of the quadrants of the framework.

Cases

Four cases are described in this section. We provide a brief overview of the case and then focus on the knowledge and organizational integration dimensions.

Loosely coupled/decentred and low knowledge integration

Diagnostic Labs is a small biotechnology company situated on the outskirts of Boston (MA) along the Route 128 technology cluster (see Saxenian, 1994). It is a privately held spin-out of a large pharmaceutical company. It was founded in 1989 and has 16 staff and a turnover of approximately $4m (end 2004). The company has in the past specialised in the development and production of reagents and diagnostic tools mainly for laboratory purposes. One of its recent successful projects, which is expected to gain FDA approval in 2005, has been the development of an innovative diagnostic for early detection of renal failure which, in theory, allows enough time for administering an effective drug to this often lethal condition. However, there was no therapeutic (i.e. a drug) available for treating this condition, even if diagnosed early using the novel diagnostic. Diagnostic Labs's intention was to develop such a therapeutic and co-market it in combination with their new diagnostic.

This development project constituted a first move into the area of pharmaceuticals. The strategic intent was to transform the company into a 'theragnostic' company that would combine diagnostic and pharmaceutical products for specific disease areas. The original had come from an individual who had been a friend of the board of Diagnostic Labs. In early 2004, after the board's approval, this individual, who had longstanding experience as a manager in the biotechnology industry, joined Diagnostic Labs as CEO.

As Diagnostic Labs's existing core competence was in diagnostics, and as it had no proprietary molecules that could be developed into a marketable therapeutic, it needed to partner with other organisations to take the project forward. Furthermore, Diagnostic Labs had no expertise in conducting clinical trials, the most expensive stage of drug development. The CEO thus made it known in his social network that Diagnostic Labs was searching for suitable molecules. A previous colleague of the CEO pointed out a Canadian company – Canada Pharmaceuticals – that was in possession of intellectual property rights (IPR) on suitable compounds resulting from a previous acquisition. Canada Pharmaceuticals had decided not to take these drug candidates into development as it had more promising compounds to develop and specialised in a different field. Canada Pharmaceuticals had previously taken the molecules through some pre-clinical research and claimed that the molecules were essentially ready for an IND ('Investigational New Drug') application. Talks with Canada Pharmaceuticals were initiated, with the objective to agree a licensing deal that would possibly involve the exchange of equity or setting up a joint venture.

Diagnostic Labs commissioned Bioclinical, a company owned by a business friend of the CEO, to carry out a Due Diligence exercise, This, however, showed that the preclinical data were still considerably short of meeting the requirement for an IND and needed further preclinical investment. Bioclinical incurred costs of approximately $100,000 for carrying out this Due Diligence. This cost was not actually billed to Diagnostic Labs but was informally registered as an investment towards any future project development activities and hence a share in future returns. Although such risk-taking is against Bioclinical's general policy, in this case Bioclinical's CEO agreed to advance the Due Diligence expense on the basis of his personal relationship with Diagnostic Labs's CEO and membership of Diagnostic Lab's scientific advisory board, in his capacity as an MD originally specialising in nephrology. At this point, no formal agreement was made as to how much the advance would be valued in investment terms. Under this informal agreement, Bioclinical would be commissioned to lead the clinical trials for the compounds. Bioclinical specialised in providing such services to biotechnology companies. It did not actually conduct the clinical trials; these were outsourced to other companies with Bioclinical specifying how the trial needed to be conducted.

While Diagnostic Labs tried to negotiate with Canada Pharmaceuticals to acquire the IPR at no cost, given the need for further pre-clinical work, it was also contacting the Venture Capital (VC) community in pursuit of finance for the project. It was estimated that approx. $5- $8m of VC funding was required for taking the molecules through phase 1 clinical trials once an IND application had been filed. However, the uncertainty surrounding the status of Canada Pharmaceutical's pre-clinical data as well as the terms of an effective licensing agreement with that company made it difficult for Diagnostic Labs to put a convincing investment proposition to VCs.

In terms of organizational integration, the Diagnostic Labs case is an example of a loosely-coupled project. Three relatively small organisations constitute the main players, featuring different and partly complementary assets, expertise and strategies:

- Diagnostic Labs: the lead organisation with overall responsibility for the project and for providing capital. In addition to the particular project described here, Diagnostic Labs is engaged in developing a variety of other products, relying on relationships with external research partners, in particular PRO scientists.

- Bioclinical: a company specialising in clinical and regulatory consulting and execution for biotech and pharmaceutical companies. Bioclinical's CEO is a member of Diagnostic Labs' Scientific Advisory Board.

- Canada Pharmaceuticals: a biotechnology company holding the intellectual property rights to two molecules that are deemed suitable by Diagnostics Labs as development candidates for its required therapeutics.

In terms of knowledge integration, this case is an example of a project characterized by low knowledge integration across the phases and across the different groups. The original innovatory idea of the project was derived from a longstanding perceived medical need, i.e. the requirement for a drug against acute renal failure and/or sepsis. Diagnostic Labs had both a special interest in, and specific knowledge of, this as the organisation was developing a tool to diagnose these conditions. As a small diagnostic company, however, Diagnostic Labs had no past or current research

capacity to discover potential New Molecular Entities (NME) that could serve as candidates for a new drug. Due to their prohibitive costs, the firm also had no resource that could be allocated to internal drug discovery or commissioned research. It therefore had to rely on existing candidate molecules that had been discovered by third parties that, for some reason, had decided not to take them into the development stage themselves. It could do this by acquiring the IPR from these third parties whereby any further involvement of the third party was not necessary.

Loosely coupled/decentred and high knowledge integration

Nowgen is one of six Genetics Knowledge Parks founded by the UK's Department of Trade and Industry (DTI) to encourage the application of human genetics research. It is a partnership between Central Manchester & Manchester Children's University Hospitals NHS Trusts and the universities of Lancaster, Liverpool and Manchester. Nowgen's overall aim is to create a community and environment in the North West which will be an international centre of excellence for multidisciplinary research in the application of genetic knowledge to improve human health and wellbeing.

The case project is called TARGET ('TPMT Azathioprine Response to Genotyping and Enzyme Testing'). Thiopurine methyltransferase (TPMT) is an enzyme involved in the metabolism of Azathioprine (AZA), an immunosuppressant prescribed for a wide range of autoimmune diseases. Faulty or absent TPMT can predict accumulation of AZA or derivatives in the body with consequent harmful side effects. The overall aim or the project is to establish the clinical benefit of TPMT genotyping in reducing the number of adverse drug reactions associated with prescribing AZA. Secondary aims are:

- To assess the relative cost-effectiveness of this pharmacogenetic (PGx) test.
- To determine service users' and providers' preferences and valuations for this test.
- To establish a model for the introduction of other PGx tests into clinical practice.

- To examine the influences of various genetic variants on response to other immunosuppressive drugs including steroids and the new biologic agents.
- To explore the scientific rationale of the use of PGx testing by investigating genotype-phenotype interactions.

The project is using a prospective randomised controlled trial of thiopurine methyltransferase (TPMT) genotyping in the management of patients, prior to commencement of azathioprine treatment. This is the first attempt by the NHS to evaluate the introduction of pharmacogenetic testing in their hospitals. The project is led by an academic genomics researcher, and requires involvement of clinicians and GPs with a wide range of specialities who will need to use the new diagnostic tool that is being tested.

In terms of organizational integration, the core project team needs to interact with a variety of organizations. These include: clinicians who need to be recruited to provide and monitor patients for the project; the rest of Nowgen; the University of Manchester administration; NHS organisations, such as NICE and NACC; the DoH (funding body); as well as with patient groups and disease based associations. A distinctive feature of this project is the absence of a commercial motive. This means that involvement of these organizational partners is based on intangible factors. For example, patient groups and disease-based associations need to be persuaded of the healthcare benefits; NHS-related organizations the healthcare benefits and cost management opportunities; academics need to see the publication potential; and practitioners the advantages of early technology adoption. Persuading these different groups that these benefits will accrue to them depends on extensive networking activity. Those leading the project have no formal organizational power to get these various groups involved and so must use persuasion.

In terms of knowledge integration, a unique feature of this project is the absence of IPR. The pharmacogenetic tests for this project are based on previously published research related to the gene for TMPT, for which there are no IPR. The main task of this project is thus to increase the basic knowledge already in the public domain, develop it, test it and translate it into a healthcare product that provides healthcare benefits. Scientific knowledge integration comes into the equation mainly

due to the fact that Azathioprine (AZA) is an immunosuppressive drug used in the effective management of patients with a wide range of inflammatory diseases, including steroid resistant or refractory inflammatory bowel disease (IBD), rheumatoid arthritis (RA), systemic lupus erythematosis (SLE), atopic dermatitis and in the prevention of acute rejection of solid organ transplants. Any attempt to understand the full potential benefits of testing TPMT genotyping would imply the need for a cross-disciplinary approach, including a variety of clinical domains – e.g., gastroenterology, orthopaedics, dermatology, transplant surgery. Some of these groups may have worked together previously, but not all, and not with basic researchers in pharmacy and genomics.

While these different scientists and science-based practitioners need to work together in this project, the commercial functions, typical in business ventures are not involved. It is an attempt to translate scientific knowledge directly to the national healthcare provider, without commercial intermediaries.

Tightly coupled/centred and low knowledge integration

AmericanBio is one of the world's largest biotechnology companies, with 6500 employees. It has its headquarters in Massachusetts (USA) where it also has most of its R&D operations. Similar to other 'classical' biotech companies, its original specialisation was to manufacture proteins used in protein replacement therapies via recombinant DNA techniques. Today, however, the company has broadened its orientation and is developing large- and small molecule drugs in a variety of disease areas. It has become a so-called biopharmaceutical company. The case project is focused on developing a therapeutic aimed at neutralising the activity of a specific protein in the human body (called here PROTEIN). PROTEIN plays an important role in controlling wound healing and other tissue growth processes. Down-regulating the level of PROTEIN would stop scarring processes, producing a desired effect for various indications, for instance renal disease, pulmonary disease or certain types of cancers.

Work on PROTEIN within AmericanBio is based on earlier work within a company called Bio-Surface which AmericanBio acquired. Bio-Surface was integrated into the small tissue repair division of AmericanBio. Clinical studies on diabetic foot ulcers were initiated, but work on chronic wound healing was

subsequently discontinued for strategic – i.e. market-related – reasons. This was because a wound-curing product would need to be sold to thousands of nursing homes – a very fragmented market. Nevertheless, one of the key proponents of the project, John P, a Senior Vice President, who had longstanding experience and interest in this field, sought to deploy the accumulated PROTEIN expertise elsewhere in the company. The re- initiation of the project owed much to his personal initiative.

Initially, work on this project continued informally with researchers in the company who were interested in the PROTEIN mechanism investigating antibodies and soluble receptors. The funding for this work came from discretionary funds and represented skunk work, mostly driven by John. Work was pursued in collaboration with academic collaborators, mainly 'paid' for by the exchange of materials. Renal disease was one area where it was thought a PROTEIN antagonist would prove promising, although there were other indications that were considered to be equally possible (for instance, cancer). In 2000, following the influence exerted by John, the project formally became a development project. In that year, an agreement with UKBio, a British biotechnology company with 270 employees, was also concluded. UKBio possessed the IPR to two specific antibodies which had been identified by the AmericanBio scientists as the most promising available candidate molecules. In 2003, another clinical trial was started but efforts to advance the 'basic science' were still ongoing, often now through formal sponsored research agreements with academic departments. By 2004, $32m had been spent on the project.

In terms of organizational integration, AmericanBio is collaborating with UKBio in an attempt to explore the role of UKBio-owned antibodies in the PROTEIN mechanisms. Although the project is run jointly, AmericanBio has responsibility for the majority of tasks, such as regulatory filings (IND) and the manufacturing facility. There is a joint Steering Committee that meets quarterly in face-to-face meetings with one phone conference in between. Core teams at AmericanBio and at UKBIO together form the PMT (programme management team). The core team on the Americanbio side consists of approximately 15 people, including employees from: science, clinical, medical and regulatory affairs (MRA), manufacturing, business, sales and marketing, legal, and finance. Most team members are involved in multiple projects and the team meets twice a month.

The project is overseen by various committees that exist to make stage-gate decisions. Most importantly, the Research Board (science-related) and the Portfolio Management Committee (commercial) review the project regularly and determine whether the project should be continued or stopped. Other bodies, such as the science peer review group (SPRG), support decision-making. The SPRG comprises the senior VPs in science and meets every Friday and reviews a program or projects. A separate sub-team, the clinical indication team (CIS), has been set up jointly with UKBIO to search for clinical indications.

In terms of other outside linkages, external academic and clinical advisors are regularly brought in to canvass opinion and evaluate research results. AmericanBio also organizes 'panel focus sessions' with experts from around the world. The aim of these is for AmericanBio scientists and managers to explore specific issues or evaluate research/clinical data with these external experts. In addition, single project participants have built relationships with other external scientists or organisations. The rationale for these collaborations is to bring in fresh knowledge and explore new avenues for what disease indications the project could explore.

In terms of knowledge integration, the project can be characterised as an organisational confluence of various knowledge trajectories.

- The accumulated knowledge of PROTEIN, which began around 1983, published in tens of thousands of journal articles by academic and industry scientists from around the world.
- Expertise on wound healing created in Bio-Surface, a company acquired by AmericanBio.
- Individual expertise, accumulated over a 20-year career, held by John P, the primary agent responsible for initiating and driving the project within AmericanBio.
- Expertise and IPRs on antibodies held by UKBio, the partner organisation in the project

Given the internal expertise in AmericanBio, they were able to bundle these various knowledge trajectories and explore opportunities for exploiting this expertise in different disease areas. This was both an opportunity and a threat. It was an

opportunity because, given AmericanBio's wide range of disease interests, the PROTEIN project could explore various indications across divisions. However, this was also proving costly, and so the emphasis had moved to finding a disease indication where the PROTEIN antibodies would actually show an effect, regardless of whether this was the area where there was greatest clinical need or market potential – they just needed to demonstrate that the PROTEIN worked. In other words, the commercial pressures were dominating the medical need pressures. Thus, although strongly driven by a 'science-push' logic, the PROTEIN project had undergone continuous assessments from viewpoints other than science, including a market assessment and an analysis of the IP position. The market assessment included issues such as the cost of sales or distribution logistics, as well as the competition in the relevant space.

Tightly coupled/centred and high knowledge integration

The final case is also based in AmericanBio but is an example in the Tissue division where a much higher level of knowledge integration is needed. Tissue engineering and cell therapy are part of the wider field of regenerative medicine that can be defined as a set of technologies to replace, repair and regenerate cells, tissue and organs. Tissue engineering involves the use of biological or synthetic materials for this purpose. Cell-therapy regenerates tissue by using externally cultivated cells or inducing controlled in-vivo cell growth. The case study explores a project that is focusing on developing a cartilage repair product (here called ELBOW). A first generation of ELBOW is available on the market but is not profitable and AmericanBio is working on developing a second generation product that is more commercially viable.

AmericanBio acquired the IPR for ELBOW by acquiring two companies. One company was based on a European scientist's pioneering technology that would isolate the patient's chondrocytes (cartilage cells), multiply them outside the patient's body and re-implant them into the damaged tissue. The other was a small tissue engineering firm specialising in regenerating human skin. This case example, therefore, reflects AmericanBios's efforts to move into a new biomedical area considered to be a promising field for developing innovative products. AmericanBio did not need to work collaboratively with these companies, it simply acquired them.

AmericanBio faced three major problems in moving this technology into the market place – gaining regulatory approval; developing a manufacturing system; and getting user-acceptance of the technology, depending on getting surgeons to use this technology, patients to agree to it and payers to pay for it. We will consider these issues as we focus on the organizational and knowledge integration issues.

In terms of organizational integration the development of ELBOW can be characterised as relatively tightly organised within AmericanBio's Tissue Division. While the IPR were developed outside AmericanBio, it acquired the IPR and then proceeded to develop it internally through setting up a programme structure. This involved setting up several different teams allocated to different aspects of the ELBOW programme. For each sub-team, members are drawn from different functional areas within the AmericanBio's overall matrix structure. The R&D team involves staff from a variety of backgrounds: biology, biomaterials and preclinical development specialists. In addition, 'business people' (jargon for senior staff dealing with strategic business issues) and regulatory staff are recruited into the project. The team meets in weekly intervals and is run by the program manager. Smaller teams assembled for specific tasks might meet more frequently. In general, considerable efforts are made to develop various components of the project in parallel. There are quarterly review meetings for the programme as a whole, involving all team members, as well as the AmericanBio Tissue senior management and senior functional leaders. The context is provided by AmericanBio's overall matrix structure. To ensure external involvement in their work, AmericanBio has a permanent group of clinical advisors, also referred to as the 'advocate board'. The general approach to soliciting the advisors' counsel is to devise a specific product development strategy, informed by science and market considerations, and invite intensive scrutiny. All advisors are ELBOW users, and have hence an intrinsic motivation to be involved in devising future generations of the product.

If scientifically and technically the development of ELBOW has been confined to a large degree within AmericanBio, important external relationships needed to be built to facilitate, firstly, regulatory approval and, secondly, market adoption. On the first point, although collaboration among innovators and regulation officials and their academic and clinical advisors are common practice even in drugs

innovation, ELBOW required close collaboration and effectively co-production of the regulatory approval pathway.

As far as market adoption is concerned, the building of relationships with two main external groups was instrumental: the community of orthopaedic surgeons, and the 'payers' (health insurers) to ensure re-imbursement. In terms of the orthopaedic surgeons a new professional society was formed around cartilage repair, the International Cartilage Repair Society (ICRS). AmericanBio Tissue was instrumental in getting this society set up and maintains an involvement. In terms of 're-imbursement', as with any new product getting insurance cover is key to widespread adoption. ELBOW costs approx $14,000, without taking into account surgery and hospital costs. AmericanBio built a reimbursement group that worked with the payers to get insurance cover in place by including the new therapy into their policies. The result of AmericanBio's efforts were that 60% of its patients were eventually covered by their policies. At the time of writing, the company had outsourced reimbursement campaigning to a 're-imbursement' company that is paid on a formula based on approvals and payments AmericanBio receives for the product.

In terms of knowledge integration, internally the ELBOW programme involves staff from a multiplicity of disciplinary backgrounds. This is needed because this type of modern regenerative medicine combines cell therapy with the use of biomaterials and drugs to enhance tissue growth. Hence ELBOW enlists all three of the traditional medical categories that the US government regulates within separate sections of the FDA. Moreover, designing a manufacturing process for a tissue-engineered product required a high degree of interaction between the manufacturing specialists and R&D scientists, on the one hand, and between manufacturing and end-users, on the other. The problem was to scale up production of the product from single Petri dishes to the required industrial scale. This is an ongoing problem that AmericanBio is working on. However, our interview evidence does not suggest that mere multidisciplinarity within the ELBOW organisations would generate more management and collaboration problems than expected in any R&D organisation. Innovation projects in most cases involve multi-functional teams, and are focused on technically and commercially feasible goal. In this sense, ELBOW does not pose

significant internal challenges equal to those challenges that are linked to the regulation and adoption of its product.

More of the problems stem from the need to integrate knowledge with external partners:

1. Regulation - AmericanBio found that regulatory staff wanted them to use models for designing clinical trials derived from those that were usually applied to drug development, even though what they were introducing was a new product category (‘Combined Devices’). For this reason, an initial clinical trial requested by the FDA failed as AmericanBio found it impossible to carry out the study according to the agreed protocol. AmericanBio had therefore to work with the FDA and convince them to change the way they approached clinical trials with this kind of product. After these re-negotiation efforts, the regulatory authority agreed to accept clinical trial modalities that were more realistic for the new type of product AmericanBio was proposing. The agreement was that two studies were to be carried out. One of those was successfully completed, the other one was well under way at the time of writing. As the Medical director commented: ‘At the end of the day, your ability to innovate is limited by the government’s ability to innovate with you.’

2. Users - AmericanBio was needing to go to significant lengths to motivate surgeons to adopt the product. As one senior manager noted: ‘Orthopaedic surgeons really are carpenters. They break and fix bones. They use devices. They don't take care that much about the biology’. This has meant that the development and use of ELBOW is involving a significant degree of interaction with the user community. Given this need to engage surgeons, AmericanBio used a market research company, which interviewed about 75 surgeons, asking them about their practice, their use of technology and problematic issues, including AmericanBio’s technology. This information partly informed AmericanBio’s specifications of future product generations and its approach to reduce the technical barriers to therapy adoption. Lead users, many now enrolled on to the advisory board, have also been enlisted in the medical marketing efforts of the company, for instance as speakers, writers or meeting participants. These frequent users have a high interest in the development of the technology and have an intrinsic motivation to provide information on results and

expert advice. AmericanBio uses this group to convince other surgeons that this technology is worth adopting.

Discussion and Conclusions

Our findings, from both the exploratory interviews and the cases, support our suggestion that biomedical innovation can be characterized as interactive (Slappendel, 1996). It is therefore important to unpack this concept of interactivity and in this paper we have done this along two dimensions: organizational integration and knowledge integration. We have also suggested a third dimension - the institutional context – but have not explored this dimension in this paper. We briefly touch on this dimensions, however, as we discuss our findings of the other two dimensions of interactivity next.

Our findings support Powell and Koput's (1996) contention that, in an industry which is expanding and evolving, as is biomedicine, expertise and other resources will be widely dispersed across organizations, making organizational collaboration a requirement (Powell, 1998). However, our findings suggest that there are different ways to access this expertise. Thus, in relation to organizational integration we suggest that there is a need to differentiate between contexts which are loosely-coupled and those that are more tightly-coupled. In loosely coupled contexts, the focal organization is heavily dependent on other organizations – it cannot move forward with its strategic objectives alone, but it cannot or will not buy in the necessary resources and pursue R&D 'in-house'. This sets the context for networked forms of inter-organizational collaboration.

Organizations, like Diagnostic Labs, use external partnerships to achieve their product development goals, primarily because they do not conduct any basic research themselves and have chosen to adopt a strict NRDO approach ('no research, development only') (Weintraub, 2004). Nowgen similarly had to rely on external partnerships, if it was going to meet its strategic objectives. In both these cases, the most salient characteristic of these external collaborations was the heavy reliance on existing social network relationships for identifying potentially relevant external partners. For example, Diagnostic Labs did not perform a comprehensive database search for relevant IPR, but relied on a personal friend for direction to a company holding potentially promising molecules. Social networks across organisational

boundaries therefore played an important role in two respects. First, personal relationships introduce a social-capital bias into activities of knowledge identification and knowledge sourcing. In other words, social networks act as 'pointing devices' or filters that help actors to decide as to what knowledge or expertise they will choose to use, exploit and adopt. Second, the social capital (Adler and Kwon, 2002) inherent in these personal relationships also served to create and maintain trust between transacting parties even though some collaborations were pursued without explicit contracts, especially in the early phases of collaboration. The existence of trust effectively reduced the potential uncertainties affecting collaborations between small, opportunistic organisations and individuals. It underpinned the relationships between Nowgen and its collaborators, as well as the collaboration between Diagnostic Labs and Bioclinical, where work was carried out for no immediate payment. At the same time, in case of the collaboration between Diagnostic Labs and Canada Pharmaceuticals - where no direct personal relationship was present – the Due Diligence exercise uncovered that initial claims by Canada Pharmaceuticals exaggerated the value of its IPR.

In tightly-coupled contexts, where resources are centralized, while it is still necessary to bring in expertise from outside, the company can do this simply by acquiring the organization that has the required knowledge – as AmericanBio did on both the PROTEIN and ELBOW projects. These small acquired companies are then integrated into the formal structure of the much larger organization, and have to formalize project processes in ways that projects in our loosely-coupled cases did not. In circumstances where acquisition was not possible or desirable, formal collaborations were instigated but these were based on formally written contracts that specified a clear demarcation of the work to be done, as for example with UKBio. Moreover, the greater level of resources centred in these tightly-coupled contexts meant that the focal organization had more influence over external organizations. For example, AmericanBio was able to help create a professional society to facilitate diffusion of its new cartilage treatment and it was able to influence the regulatory authorities to change their clinical trials protocol. It is less likely that this level of influence can be so easily exerted in more loosely-coupled contexts, where resources

are more dispersed across organizations. This is why in loosely-coupled contexts there tends to be more reliance on the goodwill deriving from social capital.

One clear outcome of these different organizational contexts relates to how decisions are made. In loosely-coupled collaborations, decisions are made on a step-by-step basis. For example, at Diagnostic Labs questions asked were: would the molecule be toxic? What could be its side-effects? Would it be effective in treating the condition? None of these step-by-step judgements – defining what needed to be done next, or what was still missing – could provide certainty as to whether drug development should proceed or not. There is hence always a discretionary margin as to how evidence should be interpreted and whether development was promising or should be discontinued. It is the permanent negotiation of the discretionary margins that is at the centre of the collaboration between all the parties, in this case, between Diagnostics Laboratories, Canada Pharmaceuticals, Bioclinical, but also Venture Capitalists and, in a later stage, the regulatory authorities. This was similarly the case in Nowgen.

In contrast, in high organisational integration contexts, once projects are formally initiated and resourced decisions are made at designated project milestones, then they are subject to more formal project reviews, rather than being judged at each decision point. One outcome of this more formal review process, is that projects can be stopped even when the lead-protagonist wants to keep going. It is unlikely this would happen in loosely-coupled contexts, because the lead protagonist could simply find new external partners. However, what is also apparent from our cases, is that even in the tightly-coupled context where commercial and scientific scrutiny of projects is likely to be greater, it is still the case that someone can push a project or re-activate a ‘shelved’ project using skunk work. This is particularly so in the early, less formalised phases of a project. In a loosely-coupled context, the resources for this kind of skunk work are likely to be absent.

Reflecting on the difference between loosely and tightly coupled organisational arrangements, the main differentiating factor is the degree of organisational flexibility. The literature on networks as governance structures suggests that a higher degree of ‘flexibility’ is one of the primary benefits of networked organisations as opposed to vertically integrated forms of organisation

(Powell 1990). From the viewpoint of industrial organisation scholars, this is due to issues of irreversibility, resource specificity and complementarity affecting innovating organisations (Foray 1991). Applied to the analysis pursued in this paper, we can postulate that in loosely coupled arrangements, the focal organisation will tend to *source* and *exploit* knowledge or expertise that *already* exists in third organisations. Collaborating with external partners can hence be understood as an exercise of bringing together different bodies of expertise existing in specific organisations (or individuals) at specific points in times. There will often be an emphasis on the exploitation of what can be called *knowledge rents*, i.e. the exploitation of already accumulated knowledge that is 'waiting' to be exploited and has already incurred sunk costs. This can be exemplified by Diagnostic Labs' external search for a suitable molecule instead of creating the knowledge about the molecule internally. The logic equally applies to Diagnostic Lab's decision to engage Bioclinical for carrying out development, instead of building their expertise internally. Similarly, Nowgen relies on clinicians with longstanding expertise to carry out its clinical research.

By contrast, in the tightly coupled contexts of AmercianBio, there was far more emphasis on using internally available knowledge and expertise for driving the project forward. Although they have the benefit of perhaps greater stability and lower uncertainty, this means that tightly coupled contexts offer less opportunities to source external expertise but force the participants to rely on what is available. This implies that there is a larger degree of path dependency built into processes of knowledge creation and exploitation in such contexts. This can be illustrated with the differences regarding how drug development was initiated in the Diagnostic Labs and AmericanBio PROTEIN cases. Diagnostic Labs had an internally developed diagnostic tool and was looking for a complementary therapeutic, mainly for commercial rationales. The firm then attempted to source external knowledge that was suitable for achieving this purpose. By contrast, AmericanBio's PROTEIN project was not initiated with a specific disease or therapeutic market in mind. The project was initiated because the company had existing internal expertise in the scientific PROTEIN area which was leveraged by some leading proponents for launching a project. This represented something of a 'garbage can' response (Cohen, March,

Olsen 1972) to an existing potential solution, i.e. the existence of PROTEIN expertise and IPR.

We now turn to discuss the differences with respect to our second analytical dimension, *knowledge integration*, which we defined above as the degree to which an innovation project requires the integration of knowledge across a wide range of actors and communities, for instance users, patients or regulators. In the two cases we have characterized as low knowledge integration cases, while some degree of interaction across groups was needed, the actual collaboration required was minimal. For example, Diagnostic Labs identified the Canadian biotechnology company that held two potentially suitable candidate molecules and was in principle prepared to cede the rights to Diagnostic Labs. This indicates that knowledge of these molecules and their potential therapeutic benefits – and potentially other on-the-shelf molecules at other biotechnology companies and University laboratories around the world – already existed, and only had to be identified and accessed by Diagnostic Labs. Intellectual property rights on pharmacological substances – often protected by patents – usually reserve to the owner the right to exploit their ability to induce certain effects in humans that are potentially beneficial. Such IPR therefore constitutes a 'knowledge package' to be transferred across parties without the need to collaboratively generate any knowledge. This is demonstrated by the fact that Diagnostic Labs would not need the ongoing participation of Canada Pharmaceuticals once the financial details of the IPR transfer were agreed. This was similarly the case in relation to the PROTEIN project, where the work of AmericanBio and UKBio could be divided up so that each worked independently on their particular part of the project.

Moreover, no close collaboration with lead users is required for this type of low knowledge integration innovation project. The overall medical need for a specific drug can be established on the basis of common medical knowledge; and it is highly likely that an effective drug that has no competitors – potentially Diagnostic Labs' drugs - would face no major adoption problems by physicians. Diagnostic Labs simply had to decide whether the scientific risk of developing these particular molecules was worth pursuing. This was equally the case in relation to the PROTEIN project.

High knowledge integration projects are very different to this – they are characterised by intense ongoing collaboration between the various parties and most importantly between parties that have not traditionally worked together before (Tuomi, 2002). One reason for this need for intense interaction is because the clinicians that will eventually use the new product or treatment practice need to actually change their behaviour, unlike in the low knowledge integration examples. Thus, in relation to the Nowgen project, clinicians need to start to genetically test patients, a practice which they have not previously done. In the AmericanBio ELBOW case, orthopaedic surgeons had to move from being 'carpenters' to being 'biologists'. There was therefore a need to create a new community of practice (Lave & Wenger, 1991) that would be receptive to the new product or treatment being developed.

For these high knowledge integration contexts, our early findings suggest that an especially important facilitator is labour market mobility (Zucker & Darby, 1997). What is required are individuals who have worked across different professional, if not disciplinary domains, and so can translate and integrate knowledge. Our evidence suggests that this labour mobility is greater in the US, with interviewees reporting greater availability of scientific 'entrepreneurs' in the US than the UK. Thus, in the US, clinicians with dual careers in clinical practice and industry, or research scientists with commercial training and hybrid professional identities (e.g. in medicine and commerce) were seen as legitimate. In contrast, in the UK, professional identities/values were more narrowly tied to *either* science, *or* medical *or* commercial roles. We also found limited evidence of venture capitalists with more scientific training in the US than in the UK and stronger networks with lead scientists (e.g. through PhD training).

These findings suggest that the US context is more supportive of *integrative capabilities* (i.e. the movement back and forth between basic science and industry – cf. Owen-Smith et al, 2002) which support knowledge integration. This has implications for UK policy, which is typically aimed at knowledge transfer (e.g. connecting or 'bridging' science and industry). However, without addressing the problems of distributed professional practices, this is unlikely to have significant impact. For example, our evidence suggests that 'translational' funding is often

simply appropriated to support existing scientific research. An alternative would be to develop policy centred on 'bonding' (e.g. creating shared incentives and opportunities for joint practice and career mobility) rather than 'bridging' (Newell et al., 2004).

While there are differences between the projects as discussed above, there are also some important similarities. With the exception of the Nowgen project, all the other cases discussed in this paper have been heavily influenced by commercial as well as scientific evaluations. Indeed, in many cases, the commercial interests dominate the scientific. This should not perhaps be surprising, given that all the cases except Nowgen, involve for-profit business organizations. However, they do illustrate the point that is increasingly being made about the wasted effort that is going into biomedical innovation, at least in terms of the impact on the overall health of society (Goozner, 2004). A related feature of all the projects was the science-push rather than medical-pull. Even in the high knowledge integration contexts where medical practitioners were involved, it was more to persuade them of the benefits of the new technology than to actually work with them to develop technologies that they themselves were desperate for. Again, it was the science-push in combination with a good commercial evaluation that was more influential than medical need.

In conclusion, biomedical innovation can be characterized as interactive. However, it is now important that we identify different aspects of this interactivity if we are going to further develop our conceptual understandings of these complex innovation processes. This paper has contributed to this conceptual development. While the analytical framework that we have developed will need to be refined, it does provide a starting point for characterizing differences across interactive innovation projects that have policy and management implications, as well as fostering a better academic understanding of biomedical innovation.

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