must be an endogenous, communitive, long-term process," says Rosiello. "It is about more than simply throwing money at it."

With European funding, SE had the luxury of being able to take a long-term, systematic approach and build its cluster from the ground up. Rather than trying to attract businesses from elsewhere, SE worked on assembling a biotech community from elements that were already in place. It provided financial support and industry training for small start-up companies emanating from the region's universities. It enlisted a local population of small, low-risk investors, who were encouraged to seek out university-based business opportunities by initiating a programme of co-investment funds, doubling the investment for suitable projects. A deficit of business managers in the region prompted SE to track Scottish executives working abroad and entice them back to the emerging network.

But strategic regional innovation systems need to understand the sector as well as the region, says Rosiello. In biotechnology, product development takes eight to ten years - much longer than in ICT - and requires five to ten times the investment. SE is therefore continuing to fund the network's growing companies beyond the initial start-up phase.

The result is that Scotland's biotech cluster is now jostling for second place in UK behind Cambridge, and has reached a stage of development where it is now attracting multi-million-pound investment from the pharmaceutical giant Wyeth.

But at a time when an interdisciplinary, systems biology approach is widely seen as the way forward through the forests of data generated by genomics, clusters built around the life sciences alone might not be enough.

"Modern biotechnology has interesting challenges and great growth potential at the disciplinary interfaces, something of which university research biologists are firmly aware in the laboratory, but which may not have been fully realised in the economy," says Cesagen's Phil Cooke.

He has shown that biotechnology and ICT are already clustering together in places such as San Francisco's Bay Area and Boston in the US, while in Europe, similar initiatives are being discussed between agricultural biotechnology institutions and automotive engineers over the development of biofuels.
One day, he says, the notions of industrial sectors and traditional academic disciplines might be as redundant as each other.

The ESRC Genomics Network (EGN) is dedicated to examining the social and economic consequences surrounding the development and use of the science and technologies of genomics.

The EGN includes 3 ESRC funded Genomics Centres - **Cesagen, Egenis** and **Innogen** – and **the Genomics Policy and Research Forum**. These investments range across 5 universities, and involve over a hundred researchers, from professors to PhD students, as well as administrative and support staff and a rotating cast of visiting research fellows. The Network is one of the largest social science investments in the ESRC's current portfolio, and is growing into the largest concentration of social scientific research on genomics in the world.

**For further information visit www.genomicsnetwork.ac.uk or contact:
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Innovation and Evolution in the Life Sciences

Change is the norm. Lakes become swamps, swamps become forests, and forests get turned into firewood and maybe even cures for diseases.

Innovation and evolution have a central place in the life sciences. After all, the whole of life on Earth is the result of an evolutionary process that feeds off the raw materials provided by mutation and recombination. The evolutionary process that interests researchers at the ESRC Genomics Network (EGN), however, is the one that underlies the life sciences themselves and the industries they support.

Science is by its very nature an evolving entity. Old models, theories, and hypotheses regarding the nature of the material universe, and the instruments and techniques used to explore it, are constantly being superseded and refined. Developments in the science are exploited by industry, which itself generates materials and knowledge that feed back into the science.
The result, to a greater or lesser extent, is improvements in humanity's ability to manipulate the universe to its own advantage - to produce food, to extend lives, and make our lives easier and more interesting.

There is no doubt that genomics is a significant evolutionary leap. It has produced forests of data - three billion base pairs of it for one human genome – and continues to pump it out at an increasing rate: data from more people and other species; data on the expression of genes within the genome and their interaction with other cellular machinery.

In that respect the so-called Genomics Revolution has been just that. But in terms of the therapies, drugs and cures it promised, it has been a bit of a disappointment. Collecting the data is just the start; the challenge now is to work out what to do with it all.

In rising to that challenge, science is reorganising. That is a social process as much as a scientific one, and it is being tracked by the sociologists, philosophers and economists of the EGN.

Integration Integration Integration

The imminent transformation of medicine that we heard so much about in the build-up to the completion of the first draft of the human genome seems a more remote possibility six years after the event. Rather than being at the base of a linear process that builds organisms via proteins, the genome is emerging as a part of a dynamic, integrated network of biological activity involving interactions and feedback loops between genes, proteins and other cellular components. And complex things, as every meteorologist knows, are very difficult to predict, let alone manipulate to one's advantage.

Many see the emerging field of systems biology as the best way forward. Systems biology sets out to tackle that biological complexity in its entirety by integrating the wealth of genomic and proteomic data with experimental findings on particular molecular interactions. Its ultimate goal is to construct mathematical models of biological systems that span cells, tissues and entire organisms.

"It's only with systems biology that scientists are taking the first faltering steps towards really confronting complexity in real systems rather than abstract ones," says Egenis director and philosopher of biology John Dupré.

Any new discipline provides food for thought for both the scientists who are working out the best way of going about things and philosophers of biology wanting to understand the nature of the knowledge generated by those new ways. Through the dialogue that Dupré and his colleagues have established with systems biologists, each can learn from the other. These discussions have allowed the Egenis team to identify radically different approaches within the systems biology community. While some biologists model systems from the top down, treating them as special, emergent levels of biological organisation, others view them as collections of chemical components to be modelled from the bottom up.

It remains to be seen, however, whether any models of complex biological systems have predictive power. “We hardly even know whether you can do science for truly complex systems,” says Dupré.

Elsewhere, the field metagenomics is exploring how systems of genomes belonging to many different species interact on an ecological scale by applying sequencing techniques to entire communities of organisms recovered from environmental samples. The technique is already being applied to microbial communities in soils and oceans, with a view to illuminating metabolic pathways that transcend species boundaries.

Even humans might better be viewed as an ecosystem of genomes. “Only 10% of the cells in the human body actually contain that human genetic recipe. The other 90% are microbes of many different species each with their own genomes,” says Dupré. “In an age when the emphasis is on *the* human genome, that’s a perspective that needs to be considered when distributing funds for medical research.” The ‘hospital superbug’ *Clostridium difficile*, for example, predominates in patients on high-dose antibiotics that kill off the very microbes that comprise such a significant part of the human organism, and many of which are an integral part of our system.

But systems biology and its related fields are integrating more than just data. The 285 names that appear at the top of the Nature paper that announced the sequence of the human genome is an indication that modern biology is a highly collaborative endeavour. Aside from the project’s sheer size, which demanded that the workload be distributed between many labs worldwide, it also required input from all sorts of molecular biologists and computational scientists who historically have worked separately. Interdisciplinary collaborations are even more apparent in systems biology, where the ranks of biologists and computer scientists are swelled by engineers, mathematicians and chemists.

The trend towards inter-disciplinary science, and the challenges it poses for scientists, is the subject of sociological research at Egenis and Innogen. It’s a trend that requires new organisational forms that transcend traditional disciplines and university departments, and demands that scientists operate beyond their particular area of expertise. The dissemination of knowledge via peer-reviewed journals also becomes problematic when reviewers with the requisite set of skills are few and far between. And while the value of many inter-disciplinary papers comes from the connections they forge between disciplines, they are often rejected on the basis that they are not seen to be at the cutting edge of any particular field.

“Inter-disciplinary research is generally seen as something that just happens,” says Innogen’s Catherine Lyall. “We’ve started talking about how you might evaluate it, build capacity, professionalise it.”

Industrial Relations

The modern biological sciences have also been driving evolutionary change in the pharmaceutical industry.

Since the late 1980s, the big pharmaceutical companies have been looking for a way out of a crisis. Their product pipelines had been drying up. The libraries of small molecular entities that had served them so well in the past were being exhausted. And stringent safety regulations meant that many of the drugs they did produce were failing clinical trials. Despite pouring money into R&D, they weren’t producing enough blockbusters.

Big Pharma’s search for a new generation of therapies was given direction by the possibilities offered by the new information technologies, biotechnology and genomics. High-throughput screening methods made it possible to screen vast populations of compounds. Also, there were early advances with large molecule biotechnology, which led to the growth of companies such as Genentech and Amgen. But Big Pharma was still chemicals-dominated, and integration of biology with chemistry happened slowly, although universities and high-tech start-ups built up expertise in risky and long-term biopharma. Big Pharma’s efforts to get in on the action set in motion a process of industrial reorganisation that continues today. Innogen researchers have been following developments closely, piecing together how change happens and what it might mean for the future of a pharmaceutical industry that, even now, isn’t out of the woods.

Without the required biological knowledge and expertise in their own R&D departments, Big Pharma companies set about capturing it from elsewhere. They started buying up small biotechnology firms and forming alliances with others. They purchased licences for particular biological compounds or technologies, and in many instances merged horizontally with complementary companies.

While fifteen years ago, up to 90% of pharmaceutical R&D was delivered internally, some companies are now buying in 40% of their product pipeline from external innovators. But according to Innogen’s James Mittra, these figures mask a new complexity in the industry. What is evolving from all those mergers, acquisitions and alliances is a dynamic network of companies of different types and sizes pursuing a diversity of operational strategies. The diversity is determined to a large extent by the variety of company-specific needs, but also by the wide distribution of knowledge and expertise in modern bioscience. “It may no longer be useful to talk about Big Pharma as a homogenous sector anymore,” says Mittra.

However, the absorption of new biotechnology-based drugs (biologics) into pharmaceutical firms’ portfolios has not had the desired effect on R&D performance. Indeed, with few exceptions, such as the breast cancer drug Herceptin, a monoclonal antibody developed by the dedicated biotech company Genentech in collaboration with the conventional pharmaceutical company Roche, the impact of biologics has been modest generally. “We still expect these new avenues to yield new therapies and make an impact,” says Mittra. “But in the longer term, and perhaps not in line with the extremely high expectations that have been held for them.”

But that’s not to say that industry’s efforts to incorporate new biological systems into their innovation processes have been wasted. “Some analysts think this process is disruptive, and that the industry is stagnating,” says Innogen’s new director David Wield. “Our conclusion is that these ventures have enabled the companies to maintain incremental, year-on-year innovation – and it all adds up.”

This incremental process has helped pharmaceutical companies survive the productivity crisis, he says, albeit with continuing pipeline weaknesses. Nevertheless, the traditional Big Pharma model based on small molecular drugs still predominates among the big companies, new blockbusters remain elusive, and biologics for more niche markets are slowly being incorporated into development pipelines.

The dominance of the multinationals is maintained by a regulatory system that makes it too time consuming and expensive for smaller companies to take a drug through all the stages of clinical trials and then to market it. “At Innogen we believe that this is an unsustainable situation, and that it’s the regulators who hold the key to change in the system,” says Wield’s predecessor Joyce Tait.

Given that Innogen researchers believe regulatory systems hold the key to radical change in health care and drug development, they are exploring how changes to regulatory systems, particularly at the most expensive Phase III stage of clinical trials, could speed up drug development and reduce uncertainty for companies. Such changes are often made possible by new life science technologies, discovery of novel bio-markers and commitment to personalised medicines, as is being explored for example in the US Food and Drug Administration’s Critical Path Initiative. If this more personalised approach to drug development becomes the norm, blockbuster drugs will no longer form the basis of the industry’s profit models and it may be possible for smaller companies, operating in niche markets, to develop their own, more independent drug development strategies.

What is certain is that any policy initiative will have differential impacts on the various players, of different sizes and with different specialities, that operate in the dynamic networks of interaction that are evolving between institutions. For example, providing public money to help small and medium sized enterprises in the start-up and early development stages of translating new research ideas into profitable products has often indirectly supported the big companies that buy them out as soon as they come up with anything promising, says Tait. Regulators and policy makers will increasingly need to take into account the complexity of new industrial innovation processes if companies are to develop the therapies that people will need and expect.

Innovating Innovation

The complexity of life science innovation – and the difficulties involved in directing its evolution through policy - is also evident in the phenomenon of clustering, whereby biotechnology companies locate themselves close to centres of academic excellence, and to each other, in order to take advantage of pools of expertise and skilled labour.

Biotechnology clusters - the focus of research groups at Cesagen and Innogen - often arise spontaneously, as in the case of Europe’s biggest, in Cambridge, which has built up over decades around the prestige university. But when, in 1999, the economic development agency Scottish Enterprise (SE) set out to generate something similar in the south of the country as part of a regional wealth creation initiative, it was starting from scratch.

There were good reasons to think that the region might be suitable for such an ambitious venture. A university sector that was strong in the life sciences was already in place, as was a network of research hospitals. Scotland’s high rates of heart disease and other lifestyle-related illness was also in its favour, in that a biotechnology industry needs a ready supply of research subjects.

But, as EGN research has shown, established clusters provide more intangible social benefits. Being in the same place allows people to meet, talk, schmooze, and build trusting relationships that facilitate the exchange of knowledge and know-how. Investors and industry consultants are drawn to them for similar reasons, preferring to work with companies they can meet in person. These social networks take time to develop - time that is rarely available to governments requiring returns from their policies within a term of office.

“Ignoring essential pre-conditions for the emergence of bio-clusters, such as a strong science base, an appropriate infrastructure and formal-informal networks, is likely to result in failure,” says Innogen’s Alessandro Rosiello, as demonstrated by the collapse of Scotland’s Information and Communication Technology (ICT) cluster Silicon Glen at the end of the 1990s, which had been created through the provision of governmental tax incentives to international companies. “A successful cluster