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Innovation and Speech Act Theory

Many socially desirable innovations are not forthcoming, but we don't really understand why. Market-pull theories suggest clear demand generates innovations, but cannot explain why demands for cures for cancer and non-polluting energy sources haven't produced results. Similarly, science-push theories suggest innovations emerge from basic research, but cannot explain why many innovations involve little, or no, input from science. Some innovations even exist before the science that explains how they work has been developed. Steam engines existed before thermodynamics and the Wright brothers flew before aerodynamics. Science appears to be neither necessary nor sufficient for innovation.

Technological paradigms and trajectories

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In the 1980s an alternative evolutionary theory of innovation emerged (Dosi 1982; Nelson and Winter 1982) that drew on Kuhn's idea that normal science follows shared problem-solving rules until anomalies accumulate and revolutionary paradigm shifts occur. Technological paradigms are the equivalent for innovation. Because the world is too complex to be captured by theory, innovation is uncertain and only a small proportion of all possible technical choices can be recognised and explored. The resulting trial and error experimentation generates technology-specific knowledge and problem-solving methods, with the result that innovations develop along cumulative, path-dependent trajectories, until they reach dead ends and are displaced by radical innovations that exploit entirely new problem solving strategies.

This evolutionary theory allows us to see the strengths and weaknesses of older theories. Science push theories correctly point out that fundamental knowledge can remove innovation bottlenecks and start new technological paradigms, but wrongly suggest science is necessary when problem solving routines are working well. Similarly, market-pull theories are right to pay attention to demand, but overlook the technical capabilities firms need to produce innovations (Dosi 1982). However, evolutionary theories of innovation don't yet explain why some technological trajectories emerge and prosper while others stagnate. Richard Nelson (2008) has highlighted that many of our normal explanations don't work. For example, the strong correlation between investment in R&D and innovation might suggest that differences in investment explain which technologies develop. However, the direction of causation is unclear as investments are typically based on perceptions of future success. Technologies that are unlikely to generate any pay-off aren't invested in. Similarly, the answer that some problems are just more difficult than others simply restates the question without explaining why.

Technical knowledge and speech acts

In the research I conducted at CAS, I tried to explore these questions using John Searle and John Austin's ideas about speech acts. They suggest language depends on our ability to have conscious mental states *about* the world, where the "aboutness" is referred to as intentionality. These intentional mental states have a type (fear, hope, belief, etc.) a content ('it will rain'), and conditions of satisfaction, so beliefs are true or false while desires are satisfied or not (Searle 1995). These conditions of satisfaction can be distinguished by their directions of fit. For example, beliefs have a mind-to-world direction of fit because the mind must match the world for the belief to be true. By contrast, desires have a world-to-mind direction of fit because the world must change to match the desire for the desire to be fulfilled (*ibid*).

These ideas can be used to tease apart some of the complex interactions between science and technology. As a first simplifying approximation, scientific explanations and theories are meant to be true, have a mind-to-world direction of fit and change in the light of new evidence. They are made true by facts and aim to be objective and timeless. Technology, by contrast, has a world-to-mind direction of fit and innovation processes change the world to match an idea. As such, technologies are more subjective and time-dependent. This explains why scientific explanations aim to be true for all people, at all times, and can apply to the past, but technologies are never true or false (they function or malfunction), are time-, place- and person-dependent, typically are more value-laden, and always forward looking (Searle 1995). You can't design a technology for yesterday, even if you can scientifically explain it.

This simplifying dichotomy can be made more realistic by looking at how science and technology interact within the messy, complex world of technoscience. Technological artefacts often involve many performance constraints and complex interactions between components that make the effects of large modifications analytically intractable. Because theory is a weak guide to practice, the knowledge required to design, develop, and produce artefacts is largely accumulated through trial and error (Pavitt 1987). However, knowledge from the natural and engineering sciences can guide innovation if the mismatch between simple theory and complex innovation problems can be addressed. This is typically done by simplifying the world (using technology) to create artificially purified 'experimental' conditions where theoretical assumptions hold. Knowledge gained from simplified examples guides the design of increasingly realistic prototypes as the simplifying conditions are relaxed, and experimentation proceeds from 'laboratory conditions' to models, prototypes, field tests and eventually real world applications. My research at CAS, with my graduate student Ohid Yaqub, has explored how these conditions are created during vaccine research.

HIV vaccine development

Vaccine innovation has traditionally been based on trial and error testing based on the notion that "similar problems have similar solutions". Jenner developed his smallpox vaccine after noting that cowpox infections conferred immunity. With HIV an effective vaccine has not been forthcoming after 25 years of research despite clear demand and excellent scientific understanding of the pathogen. Why?

The 'operational principle' – how a technology works – behind most vaccines is that the body's immune system clears the infection and them confers protection. Vaccines replicate this process to trigger an immune response without generating the disease itself. Using Searle's ideas about speech acts we have mapped out the 'operational principles' underpinning the HIV vaccine research process to attempt to understand why it has been so difficult. In doing so, we have mapped out how facts constructed under experimental conditions make statements true and how these facts generate reasons and explanations. This has revealed two main technical trajectories. The first is largely empirical and involves trying to either find a vaccine using a live (genetically) modified virus or using a killed whole virus. These methods are problematic because HIV is constantly mutating, creating the risk that a live vaccine might become dangerous. Similarly, if viruses are not properly killed the vaccine might actually cause infection – a risk that makes marketing a killed-virus vaccine for children difficult.

A second technical trajectory is more theoretical and involves either using a sub-unit of the virus to trigger an immune response, or infecting the patient using a viral vector that has been genetically modified to express HIV proteins and trigger an immune response. Two subunit (GP120 and GP160) and two viral vector approaches have been tried; unfortunately they have all failed in clinical trials. A sub-trajectory using DNA vaccines to insert HIV DNA into the host's cells, so that they express HIV antigens, has been suggested but carries a risk that this will disrupt important regulatory genes and cause cancer.

Within all these approaches there is a range of different technical decisions to be made that have produced a range of possible vaccine candidates. Because of the inherent uncertainty of innovation, these are tested in a formalised process of clinical trials. The first P1 tests basic safety, the second P2 tests efficacy and danger, while the third P3 establishes the clinical value of the drug. This third stage is extremely expensive and can cost well in excess of $100m. This raises a policy question about when to fund an expensive P3 trial and what basic research funding to cut to fund the trial.

In my work with Ohid Yaqub we have been mapping out the dead ends in innovation processes to try and unpack how such decision get made. Normally, vaccine innovation proceeds from the lab to trials through a series of increasingly realistic and complex models, typically involving animals. For most diseases an animal model exists or the disease is non-lethal, in which case it is possible to conduct tests on volunteers (i.e. graduate students). For HIV, the disease is fatal, and the animal models that do exist are unlike human HIV. Monkeys get SIV, which produces an AIDS-like disease, and chimpanzees can be infected with HIV, but do not readily progress to disease. The lack of animal models stops the creation of progressively more realistic scientific "facts", increasing uncertainties about candidate vaccines for clinical trials.

A second major problem occurs because there is no natural sterilising immunity associated with HIV infection: no-one who has ever been infected has ever cured themself. The virus can lie latent in the body for decades, which makes finding end points for clinical trials extremely difficult and makes comparing across experiments with different definitions of an end point complex. This latency produces a third major problem

related to the timing of trials. Because HIV infection generates AIDS after many years, trials will potentially take a very long time, which slows down the learning that is essential when developing complex technologies. A fourth major problem emerges because of the substantial genetic variation found with HIV, which means that the strains of the virus used in the laboratory can be very different from the primary isolates taken from the real world. The 'fact' a vaccine works in the lab will then tell us very little about its real world protective effect. Lastly, HIV vaccine development raises a range of very difficult ethical issues. AIDS rather than HIV causes death, so questions are raised about whether we should give up on trying to prevent infection and instead focus on producing a therapeutic vaccine that slows down the progression of the disease. Would it be ethical to produce a vaccine that doesn't prevent infection, but makes the vaccinated person less likely to pass on any infection they have? Similarly, is it ethical to abandon vaccine technologies in the West because they make organ transplants harder, when the chances of an organ transplant are remote in resource-poor countries?

In our research we have found that many of the problems facing HIV vaccine development are problems of science governance. Many research tasks would be useful for vaccine development, such as developing monkey twins, or virus typing (which is expensive because it kills monkeys), but are difficult to fund because they do not promise any advance in fundamental knowledge. When faced with difficult political and technical choices, peer review often defaults to awarding research funding based on scientific excellence, which may constrain the development of a vaccine if the bottleneck involves the co-ordination of research and the development and use of unexciting, shared research infrastructure.

The research we have been conducting is currently at the stage of using new theory to map out interactions within the research system, but it is gradually moving towards the point where the findings can be used to inform policy.

References

Dosi, G. (1982). "Technological Paradigms and Technological Trajectories – a Suggested Interpretation of the Determinants and Directions of Technical Change." *Research Policy* 11(3): 147–162.

Nelson, R. R. (2008). "Factors Affecting the Power of Technological Paradigms." Industrial and Corporate Change 17(3): 485–497.

Nelson, R. R. and S. G. Winter (1982). *An Evolutionary Theory of Economic Growth*. Boston, Harvard University Press.

Pavitt, K. (1987). "The Objectives of Technology Policy." *Science and Public Policy* 14(4): 182–88.

Searle, J. (1995). *The Construction of Social Reality*. Cambridge: Mass. MIT Press.