Paper to be presented at:

"EMAEE 2011: 7TH EUROPEAN MEETING ON APPLIED EVOLUTIONARY ECONOMICS
February 14-16, 2011"

Sant'Anna School of Advanced Studies, Pisa

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A problem centered approach to (radical) innovation: Insights from an empirical study of the development of an HIV vaccine

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Abstract

In this paper we propose a problem-centered approach to innovation that should better handle the uncertainty which surrounds technical change. The current literature considers that technical change is mainly about a process of uncertainty reduction and, consequently, it has proposed a variety of learning models to deal with it. Critical for the way these models conceptualize uncertainty and deal with it are their assumptions on rationality. In this respect we can distinguish three models labeled as Mr. Optimizer. Mr. Satisfier and Mr. Skeptical. While the first generation of search models, hereby labeled as Optimizer, assumes almost (unrealistic) Olympic individual capacities to deal with uncertainty (they can relate solutions to problems through information gathering activities and these search processes lead to an optimal solution), the second model, Mr. Satisfier, who builds on the bounded rationality program, introduced by H. Simon at the Carnegie Mellon School, argues that search is bounded due to memory and cognitive constraints so that search processes are "satisfying". A third breakthrough, proposed by Mr. Skeptical, consists in a new interpretation of the bounded rationality hypothesis. Mr. Skeptical contests the views expressed by the two previous models, and argues that we should conceptualize the uncertainty which surrounds technical change based on a more historical and empirical understanding of how technologies evolve as opposed to relying on some abstract notions. Alongside this hypothesis it is argued that technical change has a logic of its own (e.g. it follows certain patterns or directions). A whole

new vocabulary has been introduced to define how the TLO hypothesis can help deal with the uncertainties surrounding technical change and this hypothesis has generated different approaches (which include the product life cycle, the technological paradigm and the techno economic paradigm). As, in all the models, proposed by Mr. Skeptical, it is assumed that there are some general patterns of problem solving along which technical change occurs, we can argue that the later represent some general form of heuristic (in this way Mr. Skeptical supports the bounded rationality hypothesis although a weak one in the sense it is not possible to relate outcomes to problems, e.g. the solution to problems at hand are not contained within a knowledge representation because technical change is not predictive).

However, two theoretical puzzles remain untackled by the application of the bounded rationality hypothesis to studies of technical change. Reflecting the fact that the bounded rationality hypothesis has not dealt very well with the concept of uncertainty or radical innovation because the later imply true novelty (e.g. solutions not contained within a knowledge representation), the current applications of this hypothesis to studies of technical remain insufficient in relation to this issue. In addition, and this is a second critique which can be extended to other types of innovation, the prescriptive dimension, based on a realistic and empirical to how to accelerate the discovery of solutions to innovation problems faced by institutions/firms is still rather weak. Indeed, although Mr. Skeptical shows the existence of some patterns of problem solving across different stages of technical change, the latter tend to be very general, abstract, and low in prescriptive value. Further, the issue of how to accelerate the discovery of solutions to innovative problems is lacking.

In order to deal with these two issues we propose a new way to stretch the bounded rationality hypothesis. It is argued that a methodology that explicitly links type of innovation (associated with distinctive stages of technical change) with class of problem should help move our understanding forward. If we can associate different types of innovation with class of problem, it is argued that by looking at the processes through which these problems are solved, it may be possible to gain some insight into how to organize the learning processes necessary to support the discovery of a solution to an innovation problem at hand. We propose such a methodology here and ground our work in an empirical study of the development of the HIV vaccine. Results show that the bounded rationality hypothesis can deal with radical innovation and contribute to some extent to a more prescriptive dimension of technical change. In the sense that Mr. Satisfier supports the application of a stronger version of the bounded rationality hypothesis to studies of technical change (e.g. a more prescriptive view of technical change) we argue based on an empirical evidence for a revival of the Carnegie Mellon School program.

1. Search models: from the 60's to nowadays

As a first step we will review the three search models that were proposed in the 60's to deal with uncertainty. Critical for the way they handle uncertainty is their assumptions on rationality. As such in order to tackle these two puzzles we need as a first step to make the conception of rationality underlying these models more explicit. These models have been labeled as Mr. Optimizer, Mr. Satisfier and Mr. Skeptical. By doing so we will be able to uncover key assumptions of these models and understand where the gaps lye and to frame crucial questions which will enable us to move forward.

1.1. Mr. Optimizer, Mr. Satisfier views on technical change

Search models emerged in the 60's out of a critic to neo classical models account of technical change that treated technical change as a black box and their primary goal was to propose new ways to endogenise technology and technological change (Arrow, 1961; 1969; Atkinson, A.B., Stiglitz, 1969; Nelson and Winter, 1977; Nelson and Winter, 1982; Dosi, 1982, 1989; David, 1975, David, 1985a; 1985b, 2001); Arthur, (1989, 1994); David, P.A. et al., 1992,David, 2001). These models argue that one fundamental aspect that has to be taken to endogeise technical change is to account for the uncertainty which surrounds it (Nelson, 1959; Arrow, 1962, 1969; Sigler, 1961; Evenson and Kislev, 1976; David et al, 1992, Arora and Gambardella, 1994, Arrow, 1974). This is because firms face uncertainty about outcomes we need to take into account the processes whereby this uncertainty is reduced. In order to conceptualize uncertainty and propose ways to deal with it, search models build on different rationality programs, the substantive rationality program for Mr. Optimizer and the procedural rationality program for Mr. Satisfier . However, due to the assumptions on rationality to which both programs subscribe, it is implicitly acknowledged in both models that technical change is predictive. Mr. Optimizer's approach assumes that, when facing decisions, agents are *substantively* rational, e.g., they are postulated to know *ex ante* all options for technical change and their outcomes. Mr. Satisfier argues, owing to complexity and memory constraints, that although decisions are not *a priori* fully structured, agents, through search processes, have access e*x post* to a solution to the problem which is already contained within the knowledge representation. Subsequently, although they subscribe to different rationality programs, they still subscribe to the idea that the representation is given and, for this reason, that technical is predictive.

In both Mr. Optimizer an Mr. Satisfier firms face parametric uncertainty (e.g., the uncertainty about outcomes is due to the fact that firms lack knowledge on the values parameters of a technology). However, Mr. Optimizer and Mr. Satisfier propose different search processes to deal with uncertainty. They differ because, while for Mr. Optimizer adaptive behavior results from information processing capacities, for Mr. Satisfier is a matter of knowledge. In Mr. Skeptical firms need to gather information about the value parameters of a technology according to Bayes rules (Arrow, 1962, 1969; Sigler, 1961; Evenson and Kislev, 1976; David et al, 1992, Arora and Gambardella, 1994). Firms search for information about market prices and learning is a matter probabilistic updating about the values regarding the parameters of a technology. In order to account for how knowledge is set up and evolves Mr. Satisfier introduces the key concept of knowledge representation for "decision making under uncertainty" to take place (Nelson and Winter, 1982; Cohen and Levinthal,1989). In order to operationalize this concept at firm level they build an analogy between the concept of routines and knowledge representation. The knowledge representation of the firm incorporate rules which associate events with actions and payoffs. This representation includes the definition of the initial and final state associated with a "solution concept problem", the pay-offs associated with the transition states, as well as the operators which allow transforming an initial problem function into a solution concept. This representation contains the rules or routines for adaptive behavior to occur. Knowledge lies in the routines which are tacit. Routines are the genetic make-up of the firm. They evolve through the interaction of the entity with its environment through feedback mechanisms. Through this interaction we can describe the emergence of a new set of rules.

These views on technical change lead to different positions with regard to learning. With regard to Mr. Optimizer and Mr. Satisfier, as agents can calculate the payoffs for investments in technology, it is possible to derive normative recommendations about the learning mechanisms necessary to accelerate the discovery of a solution.

These models have been criticized. In both Mr. Optimizer and Mr. Satisfier uncertainty is used interchangeably with the concept of risk. Uncertainty here refers to a lack of information with regard to the parameters which characterize a problem. (Dosi et al., 1995). They exclude what has been termed as "substantive uncertainty" (Dosi et al., 1995), e.g., the fact that we may not have a representation of the problem to be deal with.

In addition they cannot account for the nature of the search processes necessary to deal with radical innovation. With regard to both search models evolution is self contained and, for this reason, it cannot account for true novelty (Marengo, 1992, 1998). In other words, even though, the problem solving approach proposes clear mechanisms for the evolution of rules such as feedback and feed forward mechanisms, the entity evolves through selection of events already contained within the knowledge representation (Heylighen, 1990). In other words the solution to a problem lies in the way it has been represented (Simon, 1969). Knowledge is viewed as stored (latent) information already contained within a representation so that no account of the production of new knowledge is provided. in the sense that firms do not produce new knowledge but they just adapt their initial representation to a problem based on their knowledge representation and information processing.

2.2. Mr. Skeptical

Mr. Skeptical contests the view that we can assume that technical change is predictable. He argues that, as we do not know ex ante the course of technical change *ex ante* or *ex pos*t, we need to describe the processes through technologies develop. Following this view, technology is defined as structure and interdependence and technological change as the introduction of new combinations into product architectures. Alongside this view, it is argued that we need to conceptualize the uncertainty that surrounds technical change based on the realistic and empirical study of technologies. As such scholars examine empirically "what is known and not known" for different stages of technical change and, based on this method, they identify sources of uncertainty associated with different types of innovation.

One of the most influential studies that have examined this issue is the one which builds on the work of Rosemberg (1969) who argues that although technical change is surrounded by uncertainty it has a logic of its own (TLO), meaning it follows some patterns. A whole new vocabulary has been introduced to define how the TLO hypothesis can help deal with the uncertainties surrounding technical change (Constant, 1974; Abernaty and Clark, 1978; Sahal, 1985; Vincenti, 1990; Dosi, 1982, 1988 Frenken & Murman, 2006; Arthur, 2007) and different approaches have emerged that "recast "the product life cycle (Frenken & Mrumann, 2006), the technological paradigm (1982, 1988), technological regime, and the techno economic paradigm (Freeman and Perez, 1988). These models distinguish different stages of technical change (from pre-paradigmatic states, to the emergence or consolidation of a technological paradigm) and each stage is associated with the emergence of a distinctive type of innovation (for example pre-paradigmatic stages are associated with radical innovation). Based on the hypothesis that technical change follows a logic of its own, the patterns of problem solving associated with the distinctive stages of technical change have been identified.

The innovation studies literature distinguishes four main stages of technical change which are associated with distinctive types of innovation. The first one designed "as pre-paradigmatic stage" underlies the emergence of radical innovation. At this stage the core principles guiding a product innovation are not known (Abernaty and Clark, 1978; Frenken and Murman, 2006). As such we face radical innovation. The second stage is associated with the emergence of a new technological paradigm or it is known as the emergence of a new product life cycle. At this stage the principles guiding an innovation are known (Abernaty and Clark, 1978; Clark and Abernaty, 1985; Henderson and Clark, 1990; Tushman, 1998; Clark, 1994; Frenken and Murman, 2006). However, we face uncertainty about the most adequate design to meet some user's demand. The only way to reduce uncertainty about technological and user needs is to create different designs and receive feedback from users. Problem solving concerns the exploration of various designs in order to identify the most adequate one. The innovation is architectural. At a later stage associated with the consolidation of a technological paradigm (or a product life cycle), we face uncertainty about the application of a dominant design to novel environment (Aberrnaty and Clark, 1978; Frenken and Murman, 2006). This is because over time only a few designs will eventually succeed. A dominant design or an exemplar which embodies many concepts which have been tested and are stable emerges. We face modular or incremental innovation.

However, these models are not adequate to deal with the two puzzles under analysis. Whereas Mr. Optimizer and Mr. Satisfier exclude uncertainty (Usher, 1934, Dosi and Egidi, 1991, Dosi et al, 1996) - because in these models the search occurs on a limited and known set of choices and outcomes as opposed to an open search landscape - the sources of uncertainty identified by Mr. Skeptical regarding the early stages of radical innovation remain poorly defined. Secondly, although Mr. Skeptical's approach has certainly been an extremely fruitful one which has prevailed over the last 40 years, it has low prescriptive value. Indeed, what we get is a very general and abstract description of patterns of knowledge production for different stages of technical change. Reflecting these gaps, the following questions emerge: can we define sources of uncertainty associated with radical innovation? Can we go a step further and identify the type of uncertainty associated with radical innovation? Should we follow Mr. Skeptical or adopt Mr. Satisfier's view to deal with this uncertainty? In other words, should we identify broad patterns of innovation that take place at this stage of technical change or should we try to find heuristics which can help solving the uncertainty faced at this stage? Can Mr. Satisfier accommodate learning in an open search landscape? Can we move to a more prescriptive, but still realistic, view of technical change?

2. A problem centered approach to innovation

This paper proposes to bring together two traditions of analysis, those advanced by Mr. Satisfier and by Mr. Skeptical, to address the two puzzles under analysis. Alongside, Mr. Skeptical, it considers the idea that we need to identify the sources of uncertainty that occur at the early stages of radical innovation. Alongside Mr. Satisfier we need to consider the nature of the "satisfying" heuristics which can help deal with innovation problems at hand. In other words, we need to stretch the bounded rationality hypothesis in new ways to develop a realistic but more prescriptive perspective of technical change. A new twist is proposed to do this stretching. We propose a methodology that explicitly links type of innovation (associated with distinctive stages of technical change) with class of problem (Pádua, 2008). This should help move our understanding forward. If we can associate different types of innovation with class of problem, it is argued that by looking at the processes through which these problems are solved, it may be possible to gain some insight into how to organize the learning processes necessary to support the discovery of a solution to an innovation problem at hand. This is a new principle because the literature on technical change considers that innovation is about problem-solving, i.e., it is about a search for solutions to problems but it does not explicitly link types of innovation with a class of problems.

In order to develop such a methodology the paper builds on two fields of inquiry not juxtaposed, the models developed by Mr. Skeptical and more recent developments produced by Mr. Satisfier. On the one hand, the combination of the notions developed by Mr. Satisfier with problem solving theory allows the specification of "what is known and what is not known" for the different stages of technology evolution and, based on this conceptualization, the types of innovation that tend to occur at these stages. On the other hand, the literature on problem solving provides a typology of problems. Borrowing from the efforts of Simon (1973), Dosi (1982, 1988) and Marengo (2001), Gavetti and Levinthal (200), Nickerson and Zenger (2004), it is possible to provide a typology of well-structured (WSP) and ill-structured problems (ISP) – decomposable or low interaction problems, complex problems, nearly decomposable problems with moderate levels of knowledge interaction and non-decomposable or high-interaction problems – and associate them with the type of innovation occurring at different stages of technology evolution.

To account for the process whereby problems/innovation are solved, the paper builds on the hypothesis that technology follows a semi-autonomous development pattern that is stretched in new ways. This is new because it considers how to define boundaries or constraints and directions for explicit problems in order to extract some general rules about the dynamics of conversion of this phase of ill-structured problems into better-structured problems. Moreover, we identify the heuristics used to solve this problem at a micro level. As such, a problem-centered approach allows a more integrated search landscape.

The typology of class of problems and types of innovation is provided in the following sections. Each one deals with the type of innovation which tends to be associated with a stages of technical change, the nature of the problem involved and the heuristics associated with the solving of that problem.

2.1. Near decomposable problems (architectural innovation) and patterns of problem solving

We argue, in this section, that in the early stages of a technological paradigm or product life cycle we face near decomposable problems. In the early stages of a technological paradigm the core principles guiding an innovation are known. What is not known is which exemplar or design will meet user's needs. In other words we know the core but not the interdependences which characterise a product architecture. A parallel can be established between this type of innovation and near decomposable problems. Near decomposable problems are problems about which we know the components and the complexity of the problem varies with the number of components and the interdependencies between systems, which are not known *ex ante* (Simon, 1969, 1973; Marengo, 2000). Those near decomposable problems are characterized by so called "recombinant uncertainty" which require a distinct set of knowledge properties such as integrative capabilities (Henderson & Clark, 1990, Flemming, 2001).

Near-decomposable problems, like complex problems, are complex in the sense that they are characterized by a very high number of sub-systems and interactions between them. Whereas decomposable systems are characterized by sub-systems which are independent of one another, near-decomposable systems are characterized by low interactions across sub-systems, which are weak but not negligible and high interactions within sub-systems.[1]

One way to deal with this type of problem, which has long been recognized, is to identify intermediate states in a search space in order to decompose the problem and significantly reduce the search space (Newell et al., 1962). One approach to finding intermediate states has been to use hierarchical problem-solving (Newell and Simon, 1972). A strategy for solving such problems has been to decompose the search space into sub-problems. Agents then associate with each sub-problem the right sub-knowledge representation and consequently apply a set of rules to solve the problem hierarchically. In other words, owing to the fact that higher levels are loosely coupled,

[1] The main theoretical findings from the approach can be summed up in two propositions: 1) in a nearly decomposable system the short-run behaviour of each of the component sub-systems is approximately independent of the short-run behaviour of the other components; 2) in the long run the behaviour of any one of the components depends in only an aggregate way on the behaviour of the other components.

we can solve sub-problems without necessarily affecting those higher levels. But would empirical results confirm this finding?

In order to deal with this issue we need to provide a conceptualization of the nature of the search processes which might occur in the early stages of a technological paradigm. The details of such conceptualization are provided in the following paragraphs.

The context of discovery in the early stages of a technological paradigm is "paradigm-bound". The technological principles are known but not their interdependencies. In order to account for how we can solve a near decomposable problems within these boundaries, we argue that there will be some general macro heuristics (e.g. because technical change has a logic of its own, there will be some general directions along which technical change occurs). In addition, based on cognitive science, which shows how near decomposable problems are solved, we argue that here will be some micro heuristics, e.g. there will some more specific heuristics which account for how search processes occurs along the more general macro heuristics. In order to specify the macro heuristics we build on philosophy of sciences. In order to uncover these micro heuristics, we build on cognitive science literature and its application to management studies. This includes the work of Simon (1969), Gavetti and Levinthal (200), Nickerson and Zenger (2004).

In order to account for the macro heuristics along which technical change occurs we build on the work of Lakatos (1970). Lakatos (1970) built on Kuhn's work (1962) but it stretched in new ways. Unlike Kun's (1962) rather rigid vision of science which viewed it as the result of alternating periods between normal/extraordinary science, Lakatos (1970) proposed the view that when a scientific paradigm cannot deal with problems at hand, the later is not immediately rejected. Instead the core of a technological paradigm is kept and scientists used new heuristics which help them digesting anomalies. Accordingly he proposed the idea of scientific research programs (SRP). A SRP typically has a hard core and a protective belt of auxiliary hypotheses, which help to deal with the anomalies that keep emerging. We propose to extend this approach to technology and argue that, in the early stages of a technological paradigm, the core is not necessarily rejected but that new heuristics emerge. We face technical research programs (TRP). Alongside this view, we would argue that the design search space is characterized by the search for and selection of new heuristics as possible explanatory hypotheses to solve the anomalies. A new unit of analysis is added to the search space: the search for and selection of a series of hypotheses, or positive heuristics. Engineers use one heuristic which eventually is exhausted and there is a need for a 'meta heuristic shift'.

At the level of micro heuristics and according to the work of Simon (1969), Gavetti and Levinthal (2000), Nickerson and Zenger (2004), agents build on experiential search and heuristic search. Experiential search refers to the fact that researchers build on past successes. Directional or local search is search guided solely by feedback or experience from prior trials. Heuristic search refers to the fact that people build on mental maps and re-categorize the problem according to the feedback they obtain through experiences.

This is a context of discovery characterized by the exploration of different heuristics and consequently by changing boundaries within a technological paradigm. Patterns of knowledge production are non-cumulative, although we do not have discontinuities.

Learning concerns the exploitation of different heuristics to reach a solution to the problem. Patterns of knowledge production for these types of innovation are non-cumulative. They are paradigm-bound but many changes to the boundaries occur within a TP.

2.1.2. Complex problems (modular innovation) and patterns of problem solving

The stage of consolidation of a technological paradigm (or product life cycle) tends to be associated with incremental or modular innovations. In this stage we know the exemplar or design that guides problem solving. The core and interdependences which characterize an exemplar has stabilized. In this stage, we face problems about which we know *ex ante* their components and their interdependencies but we do not know the values attached to the variables of the problem. This is incremental innovation. These are problems characterized by parametric uncertainty which require both investments on information gathering activities as well on learning mechanisms necessary to acquire technology and absorb knowledge. Modular innovation (which tends also to be associated with the late stage of a technological paradigm) refers to complex problems, problems about which we know the components and the complexity of the problem varies with the number of components and interdependences (Simon, 1969, 1973; Marengo, 2000).

As stated by Simon (1969), complex problems are characterized by a very high number of sub-systems and interactions between them. Complex problems are problems about which we know *ex ante* their components and the complexity of the problem varies with the number of components and interdependencies within existing sub-systems. This is then the source of uncertainty.

According to the literature there are technological trajectories which delimit the search for solutions. Patterns of knowledge production are path-dependent, cumulative and occur along one technological trajectory. Learning concerns the exploitation of technological opportunities.

2.1.3. Ill-structured problems (radical innovation) and patterns of problem solving

In radical product innovation (which is associated with pre-paradigmatic states of technology evolution), what is not known is the core, the technological principle guiding innovation. For example, work by Clark and Abernathy (1985) highlights how in the early competition between electric, wood and internal combustion engines the core technological principles were unknown.

In pre-paradigmatic states of technological evolution we would face substantive uncertainty. A way to deal with substantive uncertainty has been to introduce the analytical distinction between well structured and ill-structured problems. It has been argued by Dosi and Egidi (1991) and Dosi et al. (1995) that, when we are not able to fully represent the problem, we may face an additional source of uncertainty, termed substantive uncertainty, which refers to the fact that we do not know ex ante the full structure of the problem, in respect of its components and/or its interdependencies to enable us to solve a problem (Pádua, 2008). In this case, we may need additional information about the structure of the problem itself before being able to apply hierarchical problem solving – otherwise may not be able to adequately decompose it in a that will solve it due to lack of critical information about its overall structure.

To better clarify the implications of this analytical distinction between well structured versus ill structured, an example will be given. In order to explain this terminology more fully, let us consider two cases. Suppose two firms, X and Y, come from different sectors. Firm X wants to build an airplane and firm Y wants to build a new treatment for Alzheimer's disease. Firm X uses a known technology whereas firm Y starts from the hypothesis that this disease can be better treated through the germinal cells based on mechanisms for cell differentiation. In the former case, for firm X, science has already provided knowledge about *the scientific principles* underlying the problem under analysis so that firm has a good *representation of the problem*. It has information with regard to the *initial and final state of the problem* (such as building an airplane based on a pre-defined design), and the *state spaces involved in the search process* (all possible combinations of design, motor, wings of known sub-sets). The structure of the search space is *complex* but *finite* in the sense that it is characterized by many possible solutions which are known *ex ante* (those are already contained within the initial representation). Since the problem is well-structured firm X can optimize its production choice given time and resource constraints by the choice of an adequate set of heuristics and thereby develop a set of adaptive routines or procedural knowledge (which incorporates the capacity of adding information through the interaction of the firm with its environment).

By contrast, firm Y just knows that it has to produce a new set of differentiated cells, added to the fact that those cells will have a certain function within an organism. The *scientific principles* underlying the technology are not very well known yet, so that the *intermediate states* involved in the problem are not known (unlike the airplane we do not know that the problem involves wings, engines, etc.). In this sense the problem of firm Y is ‘ill-structured’. While the search process goes on, new representations are added to the search space, which include the addition of new states of the problem and new ways of relating those sub-systems (for example stem cells are localized in one specific zone of the brain, the mechanisms involved are related to cell differentiation). Knowledge production involves an open-ended dynamics in the sense that the search process leads to the discovery of new potential candidate solutions which are added to the knowledge representation.

In order to deal with the type of problem associated with radical innovation it is argued that the macro foundations which guide problem solving are competing technological paradigms (as suggested, by Dosi, 1982) and the micro foundations are processes related to changes in knowledge representation (as suggested by Nikerson and Zenger, 2004). The main cognitive process used to solve an ISP in different stages of technology evolution is abstraction (which involves some changes to knowledge representation), analogical reasoning and other set of heuristics.

In addition, by relating radical innovation with ill-structured problems, we might be in a position to clarify certain debates about the origins of radical innovation. While some scholars argue that radical innovation involves an open ended dynamics (Dosi’s, 1995, Cohen and Levinthal, 1997), other scholar take the position that the later is about local search (Flemming, 2001, Schomaker, Duystens, 2010). However these studies tend to be vague, abstract, as they do not rely on a detailed description of how individual inventions evolve. Neither do we know what kind of recombination occurs (within which kind of boundaries and along what kinds of directions nor how it occurs (how changes of knowledge representation occur).

To conclude, by stretching the bounded rationality hypothesis it might be possible to specify the problems associated with different types of innovation.

3. Methodology

In the following section we offer an overview case study of work being conducted in the search for an HIV vaccine. This setting is appropriate because the HIV vaccine is a case of product innovation in which the technological principles are not clear from the outset. As such it is a problem where the core is not known. It is case of radical innovation.

The methodology used in this case is inductive and relies on the mapping of dynamics of knowledge production in the HIV vaccine over a period of 15 years (1987-2002). A semantic network characterizing the relationships between concepts in he HIV vaccine search has been produced. A bibliometric analysis, more specifically co-word analysis (Callon, 1991), based on manual indexation of more than 600 abstracts, has been conducted alongside the template defined by the semantic network.

A more detailed explanation of the methodology is provided. The methodological approach described relies on the hypothesis of co-word analysis but it also introduces a new set of techniques/tools. A bibliometric analysis was conducted to study the evolution of a scientific field in terms of its content but with the support of tools from AI (artificial intelligence). AI methodologies, more specifically, semantic nets, were used to describe the structure of the technical study under study (vaccines). Semantic nets are knowledge representation techniques from AI which can be particularly adapted to this study (Burgun A, Bodenreider O.,2001),. They have a network structure in the sense that some links are displayed as a taxonomic tree, whereas others are non-hierarchical. By using semantic nets we were able to represent the field under study, e.g. to introduce there variety of approaches to HIV vaccine design as well how the later relate with components and sub-components.

We used semantic nets to give a better foundation to the co-word analysis. By combining co-word analysis with semantic nets it is possible to study the structure and evolution of a scientific domain. The semantic provided a template of what is the structure of the field (it defines the major approaches for HIV vaccine design, components and sub-components). We used this tool to conduct the co-word analysis, e.g. the bibliometric analysis of papers published in the HIV vaccine search landscape. Papers were categorized according to the approach to vaccine design used and the concepts that were employed to test these approaches. Based on the counting of the frequencies of these key words we obtained maps about how many papers dealt with one approach to vaccine design in period X, Y and Z.

4. Results

Before presenting the results we should start by defining what is a vaccine. A vaccine is defined by Parslow et al. (2001, p. 74) as a "substance that teaches the body to recognize and defend itself against bacteria and viruses that cause disease". An AIDS (Acquired Immune Deficiency Syndrome) vaccine is for the time being a hypothetical concept. But it would teach the body to recognize the human immunodeficiency virus (HIV) that causes AIDS and provoke an immune response that would defend against the virus if it entered the body thus preparing it to fight and also to remember how to fight, if exposed to this specific infection. A vaccine is not a cure, but it prevents infection or slows disease progression.

As vaccines are based on the introduction of components of the pathogenic organism into the host organism, research on the HIV vaccine focuses on research into the host's immune response and research into the HIV virus, as well as their interactions. In other words, search in the area of the HIV vaccine is based on searching for the HIV components which will produce the best results in terms of immunological response.

In order to find a solution to the HIV vaccine we face two major tasks, one dealt by science and a second one by technology (e.g., vaccines search). Vaccines are based on the identification of a small part of the virus, designed by the antigen, that will trigger an immune response. The identification of this substance is the task of science. When such a substance is identified we need to identify how we will administer it in the organism in order to activate such an immune response. This is the task of technology. Vaccines rely on combinations of the antigen, adjuvants and vectors and are based on different strategies of administrations (oral etc.).

In order to identify the small part of the virus that can activate an immune response we can look for four types of response (this is because there are four major types of immunity). Accordingly, there are four research programmes upon which scientific research can draw for the discovery of the HIV vaccine. Non-specific defence immunity leads to the 'Innate research path', whereas specific defence immune response generates three research paths called 'Humoral immunity', 'Cellular immunity', and the combination of the two 'Humoral and cellular immunity'. Humoral immunity acts by producing antibodies whereas cellular immunity activates the actions of specialized cell, called killer cells that attack the virus.

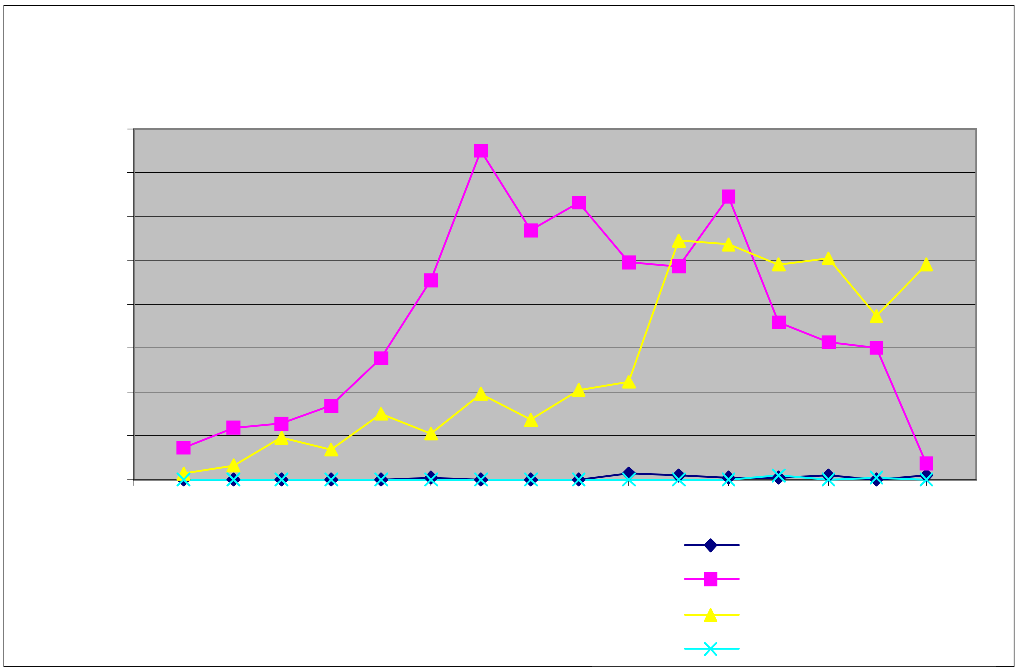
With regard to the vaccine, we can distinguish eight approaches to vaccine design or technological paradigms to deal with this problem. Each approach or technological paradigm provides a key operational principle which guides search, an exemplar and trajectories along which technical change might proceed. For example, a more recent approach to vaccine design, the so-called DNA vaccine was created, in 1985, in order to prevent Hepatitis B. The exemplar here consists in its successful application to Hepatitis B. The new operational principle of this approach consists in the insertion and expression of viral or bacterial DNA into human or animal cells (beforehand the antigen was introduced in the host through other means, researchers introduce the whole killed virus or parts of it, as done by the life attenuated approach (which contains live attenuated micro-organism). The way adjuvants, vectors are combined in DNA vaccine is completely different from other vaccine design. In this case the antigen is introduced by using other cells whereas in previous approaches the antigen is introduced "directly" with the use of other adjuvants .

Results show that the development of an HIV vaccine has gone through four periods (in the period 1987-2002). In each period the perception of what is the nature of the problem to be tackled changed over time. It is shown that the nature of the problem is associated with the stage of technical change and it determines different types of search patterns.

4.1.The HIV vaccine as a case of product radical innovation

Based on a bibliometric analysis and set of interviews with HIV experts, three distinct periods in the evolution of HIV vaccine research have been distinguished over the period 1987-2002. The bibliometric analysis relied on a database of 1309 papers which have been classified manually. The methodology used to classify these papers is co-word analysis. A total of 27,708 co-occurrences have been obtained and the frequency of co-occurrences for each period has been counted. Each period was characterized by the use of different research paths. Those periods have been identified according to one criterion: the number of co-occurrences by research paths in the scientific discovery search space. As the graph shows the first period draws on the antibody approach. The second period relies on the use of both antibody and CTL approaches. The third period draws on both approaches but the CTL approach takes off. The results obtained are shown in the next figure.

Figure 1: Results for HIV vaccine research paths



In order to account for this first set of empirical results it is necessary to provide a brief historical overview of research into the HIV vaccine. Research on the development of an HIV vaccine started in 1984. In the mid 1980s, it was thought that an envelope-based vaccine would be quickly made using recombinant DNA technology.[2] This was based on the finding that the outer envelope of HIV was important for stimulating neutralizing antibodies.

The graph shows that in the first period scientists chose the antibody approach to design a vaccine. Most conventional approaches of vaccine design are based on the induction of antibodies that attach to the virus and neutralize it. This is because the antibody is the only component of the adaptive immune response that can neutralize a virus particle prior to infection of a cell and it is the only immune response associated with protection for any currently licensed vaccines. Previous and current vaccines have proved successful for combating diseases such as poliomyelitis, measles and influenza. However this approach led to poor solutions for the discovery of an HIV vaccine.

At a certain point in time scientists changed their interest and started giving more importance to another alternative, the CTL approach. Unlike antibodies, cytotoxic T cells recognize infected cells rather than the infectious agent itself. T lymphocytes detect the presence of a foreign substance by way of surface proteins called T-cell receptors. The CD8 T lymphocytes, also called T killer lymphocytes, eliminate cells that display antigens on their surface. This is accomplished by releasing cytotoxic substances that will rupture the cell's cytoplasm leading to its destruction (through granzyme and perforin). Very few vaccines have been made based on this approach. They are mostly experimental or less effective (like vaccine BCG against tuberculosis). This approach also led to poor solutions for the discovery of an HIV vaccine. Different vaccine designs were used based on DNA and other approaches to vaccine design.

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[2] An envelope-based vaccine that would trigger an immune response via neutralizing antibodies using recombinant DNA technology (McMichael, 2003).

At a later stage another starting point considered was to use both immune antibody and cell mediated responses. Reflecting the fact that there are two main immune responses to pathogenic agents, scientists could choose one of two major options to start tackling this problem. There are two main immune responses, the humoral and cellular immunity, and there is often debate and speculation about which component of the adaptive immune system is most important for immunity. Many vaccines rely on both approaches. But the results were not very encouraging either. In other words scientists and engineers tried to put two things which do not work well together. All sorts of vaccine design were used by that time, peptide, sub-unit, DNA vaccine etc.

A fourth approach was the search for radical new strategies for vaccine discovery (2002 onwards): the humoral and cellular research path versus the innate/acquired path as distinct explanatory hypotheses to account for correlates of immunity within the scientific discovery search space. Vaccine designs are based on the search for radical new scientific approaches and new combinations of technological heuristics due to persistent functional failure. Again all sorts of vaccine design were experimented.

4.2.Problems/stage of technical change and type of innovation

Nowadays, the idea that the HIV vaccine involves a radical innovation is well accepted. However, this was not evident at the beginning. This section examines the different perceptions on the type of innovation associated with an HIV vaccine until it became evident that production of an HIV vaccine is a case of product innovation in which the technological principles are not clear. The respective problems that are associated with different stages are identified.

Research on an HIV vaccine started in the mid 1980s after HIV was characterized in 1983 in terms of its genomic structure and protein functions. Recognition of the need for an HIV vaccine emerged soon after the virus was discovered (Barre-Sinoussi et al, 1983), but it was not immediately recognized that this would require a radical innovation. In the mid 1980s it was believed that its development would be relatively straightforward. Indeed, when R. Gallo from NIAIDS was asked in 1984 by Reagan's administration how much time it would be necessary to develop an HIV vaccine, he answered that this task could be completed in two years.

In the early stages of vaccine development, scientists and engineers thought that the problem of the HIV vaccine involved just some technical puzzles. More specifically, it was believed that an envelope-based vaccine would trigger an immune response, via neutralizing antibodies using recombinant DNA technology (McMichael, 1998). On the scientific side, it was considered that the correlates of immunity were known. This was based on the finding that the outer envelope of HIV was important for stimulating neutralizing antibodies.

The boundaries for search were defined by the DNA technological paradigm for vaccine design which had been successfully applied to the envelope-based Hepatitis B vaccine. A great deal of search with the goal of identifying a new configuration but within the boundaries of a technological paradigm, was conducted through to the beginning of the 1990s. The search was about the identification of the interdependences between systems that would trigger an immune response. The possible combinations were enormous. There are more than 20 adjuvants possible, there are also a high number of potential vectors for vaccine design that could be used. We were facing a near decomposable problem.

Then scientists and engineers realized that the problem of the HIV vaccine involved some technical anomalies. Moreover, it was becoming more and more evident that, due to the persistence of technical anomalies, the HIV vaccine posed both technical and also many scientific challenges. This is because the HIV vaccine is characterized by features that are missing in other more conventional vaccines. These features have posed serious difficulties for the application of more conventional approaches under these new more stringent conditions. The core principle for vaccine design was not known.

It became evident that the problem was ill-structured, e.g., neither the core or component guiding search were known. Since 1984, key advances in basic research have clarified the science guiding the HIV vaccine, but so far the knowledge produced by science does not provide a sufficient base to guide the transition from a theory to an application such as the vaccine itself. Although science helps in delimiting partitions of the search space pointing out important areas of research that need to be explored and exploited, the knowledge representation of the problem is still partial. Research involves the search for the right representation of the problem. It may be necessary that the most adequate knowledge representation of the problem is built first before it can be converted into a heuristic problem.

4.3.Dynamics of knowledge production

The next issue to be tackled concerns the issue about whether we can find some general patterns of problems in vaccine search We will examine this issue for the two stages of vaccine development.

At the early stages when it was thought the problem was near decomposable scientists/engineers used different heuristics in order to identify the new set combinations which could lead to a solution to the problem.. These heuristics helped researchers to look for the combinations of antigen, vectors and adjuvants which would be more likely to trigger good results.

The core is known and in order to protect the core scientists use a protective belt of hypothesis to “digest” anomalies. As such different technical research programs are used. Search occurs alongside these heuristics. At micro level firms rely on heuristic (re-categorization of the problem) and directional search to find new combinations for the problem under analysis.

The design search space is characterized by the search for and selection of new heuristics as possible explanatory hypotheses to solve the anomalies. A new unit of analysis is added to the search space: the search for and selection of a series of hypotheses, or positive heuristics. Engineers use one heuristic which eventually is exhausted and there is a need for a ‘meta heuristic shift’.

However, as the envelop based DNA vaccine did not lead to the eagerly awaited solution, scientists/engineers turned to other approaches. In the late 80’s, 90’s an approach that was envisaged was the life attenuated approach. However**, t**he life-attenuated approach has been only rarely used for vaccine design. This has generated some significant controversies. For example, the life-attenuated approach is the only one that has produced an ‘experimental proof of concept’ that an HIV vaccine might work (some monkeys have been immunised successfully through this approach) was viewed as too dangerous. An important controversy was generated about the possibility of NIAIDS engaging in small-scale human trials based on this concept. It has been disallowed due to fears of virus mutations.

At this stage scientists engineers engages in all sorts of trials which relied on different paradigms or vaccines approach (Faucci, 1996). We entered a phase of competing paradigms (Dosi, 1982). Micro heuristics include analogical reasoning, re-categorization of all sorts (Nikerson and Zenger, 2004).

5. Implications of a problem centered approach to studies of technical change

The papers started by raising two puzzles regarding the application of the bounded rationality hypothesis to studies of technical change. An approach was designed and empirical results were obtained through the case study of the development of an HIV vaccine. We will now discuss the implications of the empirical results to the issues we raised. Section 1 discusses the implications of the empirical results to puzzle 1 whereas section 2 examines the second puzzle.

5.1. Can the bounded rationality hypothesis be stretched to radical innovation?

One of the major criticisms that has been raised regarding the application of the bounded rationality hypothesis to studies of technical change has been the fact that the later cannot account for true novelty. This is because the later assumes that agents are equipped with the right representation of the problem (options of technical developed and outcomes are known *ex post* through search processes). However, true novelty involves an open ended dynamics, e. g., the identification of new events not contained within the initial representation. Empirical results show that although technical change is characterized by an open ended dynamics it is still possible to identify heuristics at macro and micro level that help dealing with the uncertainties which surround technical change. We hereby list the major findings.

The first finding is that radical innovation corresponds to an ill-structured problem. This is new because this association between class of problems and types of innovation had not been made before.

The second finding is that technical change involves an open ended dynamics. As stated by Dosi (1995), e.g., new solutions not contained within the initial representation are added to the search space. This is because what was once thought to be a resolution of a sub-problem or a puzzle turns out to be only a partial solution and the puzzle needs to be re-opened. These are open-ended dynamics.

At macro level we have competing paradigms or different approaches are used to find a solution to the problem (Dosi, 1982). Considerable changes in knowledge representation are needed in order to find new solutions to these puzzles. This case of problem-solving requires local search but also long jumps e.g. radical re-categorizations of the problem (Dosi, 1995; Levintal, 1997).

The third finding is that changes of knowledge representation is guided by the search and selection of an approach. Competing paradigms or approaches are used. At micro level different heuristics such as analogical reasoning is used.

Summing up, we have provided a conceptualization to account for the nature of the uncertainty and the search processed which characterize the early stages of radical innovation. Empirical results have confirmed the validity of such representation. In that sense, we might argue that we provided a representation with higher explanatory power than previous approaches (which argued that radical innovation is characterized by an open ended dynamics but without specifying the boundaries or directions along which the later occur). Furthermore, we have shown that radical innovation involves local search and long jumps (so in relation to the debate about whether it involves local search or long jumps we would argue that it involves both). However, bearing in mind the fact that we built this research based on one case study, the issue which emerges concerns the generazibility of results. We would need more case studies to confirm the conceptualization of technical change hereby proposed for radical innovation.

5.2. Can a problem centered approach to innovation support a more prescriptive view of technical change?

The second puzzle that we put forward concerns the possibility of applying the bounded rationality hypothesis in new ways in order to obtain a more prescriptive approach to technical. Beforehand we should note that, alongside Mr. Skeptical views, results show that a very strong interpretation of the application of the bounded rationality hypothesis to studies of technical change is not possible(e.g., it is not possible to relate outcomes to solutions through the use of heuristics because technical change is characterized by unforeseen events). For this reason, the possibility of ever developing a strong prescriptive approach to technical change is almost an impossible task. However, despite such strong constraints, results show that it is possible to stretch the bounded rationality hypothesis in new ways that may support the development of (a limited) prescriptive approach to technical change. Two new paths are hereby suggested.

The first way in which we could stretch the bounded rationality hypothesis concerns the idea that it might be impossible to recognize the problem we are facing much earlier on. Already in 1987 it was known that the HIV vaccine was an ISP and that there would be value in promoting a variety of approaches towards HIV vaccine discovery (an an ill-structured problem would require). But, from the early 1980s up to the late 80's, the focus was on a single approach. Would the process of discovery have been quicker if the focus had included a variety of approaches from the beginning, in different technological programs?

If that would be the case and according to the conceptualization we provided in this paper scientists/engineers should have invested right away in several technological paradigms and on a variety of key problem solving capacities (involving analogical reasoning etc). Would that be a way forward to develop further the bounded rationality hypothesis?

In order to deal with this question we would need more case studies in order to identify whether the conceptualization of radical innovation as an ill-structured problem is supported by empirical evidence. However, it should be noted that, possibly, one of the advantages of this study is to show that scientists/engineers have their own biases when conducting research. Making these biases more explicit can be an advantage. Once these are recognized we can move forward and try to frame problems in a more "objective" way.

In addition, the second way whereby we might consider extending the bounded rationality hypothesis regards the possibility of developing a less abstract and general approach to search processes. While Mr. Skeptical's ideas has represented a key breakthrough in studies of technical change, the search processes that are used to account for how technologies evolve are too general and abstract. The idea that technical has a logic of its own might be interesting but we may need additional information on how this proceeds. Possibly, the key insight of this study is to argue that we can develop the TLO hypothesis in more specific ways. Instead of using the TLO hypothesis to describe general processes of technical change that apply to all sorts of innovation, we showed that this hypothesis might apply in different ways for different types of innovation. In addition, by specifying the micro heuristics which are used to solve problems we can obtain a much less abstract understanding of processes of technical change. We have confirmed this possibility both for radical and architectural innovation. But would these results be generalizable? Could these principles be applied to other types of innovation (modular and incremental innovation)?

In order to deal with these issues we would need more case studies.

6. Conclusions

The paper argues that a problem centered approach can support a more prescriptive view of technical change and an understanding of the dynamics of knowledge production which take place in radical innovation. The current approaches to deal with uncertainty have been reviewed. It was shown that the application of the bounded rationality hypothesis gave rise to two very influential approaches to deal with the uncertainty which surrounds technical change, a strong version where it is assumed that individual can related solutions to problems through the use of heuristics and a second one, a weaker version, where it is argued that we can only hope for an understanding of the very general heuristics or directions of technical change (without necessarily knowing how to relate solutions to problems). In addition, none of these approaches was able to account for the emergence of true novelty which is key to account for radical innovation. We argued that a problem centered approach which takes into account insights of both Mr. Satisfier and Mr. Skeptical could help us to deal with the two puzzles identified. Empirical results grounded on an empirical study of the development of an HIV vaccine shows that the bounded rationality hypothesis can account for true novelty (although with some limitations). Secondly, we propose two new directions of search to improve the prescriptive dimension of technical change. The first one refers to the fact that it may be possible to recognize quite early what is the nature of the problem at hand and organize search accordingly. The second one is that it is possible to develop a less abstract and general application of Mr Skeptical approach by specifying the general heuristics which characterize problem solving for different types of innovation (instead of one heuristic which applied to all sorts of innovation). Secondly, by relating classes of problems with types of innovation we can identify the types of micro heuristics which can help dealing the innovation problems at hand. In other word by combining in new ways the approaches underlying Mr. Skeptical and Mr. Satisfier we hope to have proposed a model to account for patterns of problem solving with a higher explanatory power and with prescriptive dimension.

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