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A triple helix model of medical innovation: *Supply*, *demand*, and *technological capabilities* in terms of Medical Subject Headings

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ABSTRACT

We develop a model of innovation that enables us to trace the interplay among three key dimensions of the innovation process: (i) *demand* of and (ii) *supply* for innovation, and (iii) *technological capabilities* available to generate innovation in the forms of products, processes, and services. Building on triple helix research, we use entropy statistics to elaborate an indicator of mutual information among these dimensions that can provide indication of reduction of uncertainty. To do so, we focus on the medical context, where uncertainty poses significant challenges to the governance of innovation. We use the Medical Subject Headings (MeSH) of MEDLINE/PubMed to identify publications within the categories "Diseases" (C), "Drugs and Chemicals" (D), "Analytic, Diagnostic, and Therapeutic Techniques and Equipment" (E) and use these as knowledge representations of *demand*, *supply*, and *technological capabilities*, respectively. Three case-studies of medical research areas are used as representative 'entry perspectives' of the medical innovation process. These are: (i) human papilloma virus, (ii) RNA interference, and (iii) magnetic resonance imaging. We find statistically significant periods of synergy among *demand*, *supply*, and *technological capabilities* (C-D-E) that point to three-dimensional interactions as a fundamental perspective for the understanding and governance of the uncertainty associated with medical innovation. Among the pairwise configurations in these contexts, the *demand–technological capabilities* (C-E) provided the strongest link, followed by the *supply–demand* (D-C) and the *supply–technological capabilities* (D-E) channels.

1. Introduction

The development of models of innovation capable of increasing our understanding of the innovation process and of tracing/predicting innovation dynamics have been a longstanding central topic in the science-policy and innovation-studies literature as well as of policy debates (Martin, 2012). The complexity of the models of innovation proposed has increased over time: the "chain-linked" model of innovation, for example, advanced on linear models (*technology-push* and *demand-pull*) by introducing feedback and feed forward loops among the different stages of the innovation process (Kline and Rosenberg, 1986). However, such interactive models are not sufficient to explain what drives innovation and technological development, and why certain firms are more capable than others in pursuing innovation (Marinova and Phillimore, 2003). Evolutionary economists, building on nonlinear feedback analysis from evolutionary biology, have instead pointed to the role of *routines* (i.e., standardized patterns of actions representing 'genes') that firms use to develop products and services (along *technological trajectories*), which, in turn, generate *variation* (Nelson and Winter, 1977, 1982). Products and services compete in market and non-market *selection environments* (Nelson and Winter, 1977) including technological (Dosi, 1982) and technoeconomic *paradigms* (Perez, 1983).

In such a framework, one can expect more than a single selection mechanism to be relevant in the case of innovation. In his study of post-Schumpeterian contributions, Andersen (1994, p. 195) noted that "(E)volutionary economics cannot rely on a standard form of explanation to the same extent as evolutionary biology." Biological evolution theory, assumes *variation* as a driver and *selection* to be naturally given, while cultural evolution is driven by individuals

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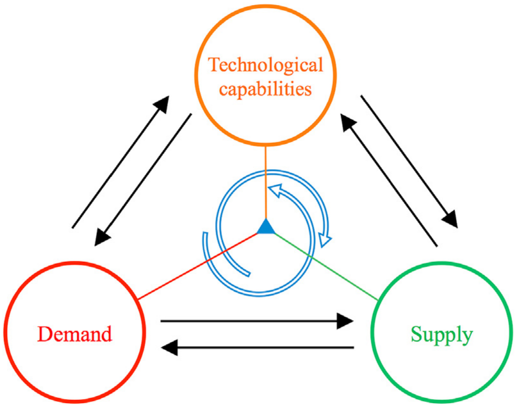

Fig. 1. Models of feedback loops based on interactions among: *supply*, *demand*, and *technical capabilities*. The directionality of the arrows represents the possibility of differential strength in opposite directions.

Source: Authors' elaboration.

and groups who make conscious decisions on the basis of potentially different criteria (Newell and Simon, 1972). As such, the evolving construct is not a given unit of analysis (Andersen, 1992, p. 14). Boulding (1978, p. 33) suggested that "(W)hat evolves is something very much like knowledge." Yet, not only bodies of knowledge are evolving, but also markets. Henceforth arises the basic question, under which conditions can the different selection mechanisms be expected to co-evolve and lead to (options for) new innovations?

When different selection mechanisms can operate upon one another, a complex systems dynamic is generated. From this perspective, the model of the National Innovation System (e.g., Freeman, 1987; Lundvall, 1988; Nelson, 1993), and its subsequent extensions to systems of regional (Braczyk et al., 1998) or sectorial (Malerba, 2004) innovation, can be considered as the specification of possible levels of integration (cf. Carlsson, 2006); but both integration and differentiation among selection environments can be expected to operate continuously in complex systems of innovation. The interactions among selection mechanisms generate options for innovation by decoding and recoding the relevant criteria (Cowan and Foray, 1997) or, in other words, puzzle-solving (Arthur, 2009; Bradshaw and Lienert, 1991).

The literature on the co-evolution between two selection environments highlights processes of mutual shaping (McLuhan, 1964), niche formation (Schot and Geels, 2007), or lock-in (Arthur, 1989). While stable equilibria are often attractors along the evolutionary pathway, pathways along trajectories can, however, become meta-stable or selected for globalization at the regime level, when three selection/variation mechanisms operate upon one another (Etzkowitz and Leydesdorff, 2000). Co-evolutions between two sub-dynamics can be continuously upset by a third, leading to crises, hyper-stability, and other complex phenomena (Leydesdorff and van den Besselaar, 1998; Ulanowicz, 2009).

Here we consider a nonlinear three-dimensional model of innovation, with a specific focus on the medical context as discussed below. Fig. 1 depicts the interactions among three key dimensions in innovation studies: *supply*-side factors, *demand* articulation, and *technological capabilities* (e.g. state-of-the-art instrumentations) to generate new products, processes and services. The triangle of arrows allows for—potentially alternating—clockwise and counterclockwise rotations and even (next-order) loops. The relation between any two dynamics can be spuriously correlated upon by a third factor, which may enhance or dampen the relation between the other two.

For example, the relation between *demand* articulation and *technological capabilities* may lead to new *supply*-side offering of products, processes or services. In other words, the relations between each two dimensions can be auto-catalyzed by the third so that proliferations or extinctions become possible when the order of the arrows can circularly be closed into recursive loops (Krippendorff, 2009a; Ulanowicz, 2009). A self-organizing complex system thus can be expected to emerge from linear flows when feedback loops continue to exist (Maturana, 2000).

For the measurement of these complex dynamics, we turn to entropy statistics (Shannon, 1948; Theil, 1972). These measures have been used in triple helix research to build an indicator of mutual information (relational dependence) among three dimensions x, y, and z, namely T_{xyz} (McGill, 1954; Yeung, 2008, pp. 59)—the mathematical formulation of this indicator will be provided and utilized as part of our analyses. Negative T_{xyz} values have been associated with the reduction of the uncertainty that prevails at the system level because of synergetic integration, while positive values can be considered as indicating differentiation among the interactions (Leydesdorff et al., 2014).[1] Leydesdorff and Ivanova (2014) showed that negative information in a triple helix configuration finds its origin in redundancy that is generated when uncertainty is selected from different perspectives. New options are generated in the interactions among selection mechanisms. The total number of options—the maximum entropy—is thus increased. The increase in the redundancy may outweigh the increase of uncertainty generated in ongoing processes of variation.

The relevance of this indicator for innovation studies can be appreciated from the two perspectives of reducing uncertainty or increasing redundancy. First, one can expect a configuration with less uncertainty to be more rewarding with regards to risk-taking than periods with high uncertainty in the relevant (selection) environments. Reduction of the prevailing uncertainty provides innovators with dynamic opportunities comparable to local niches (e.g., Schot and Geels, 2007). Note that reduction of uncertainty at the systems level provides an advantage for reflexive agency insofar as it is perceived.

Second, the increase in redundancy itself is a structural effect at the systems level—that is, a result of interacting selection mechanisms. The relative reduction of uncertainty in the configuration is caused by an increase of the redundancy in terms of the number of options available for innovation. (The two components—relative information and redundancy—are each other's complement, adding up to the maximum entropy of a system.) Among the total number of options possible, the redundancy represents the configurations which have not (yet) been realized. An increase in this number does not necessarily affect the number of the realized options as long as the maximum number of options also increases (Brooks and Wiley, 1986, p. 43; cf. Khalil and Boulding, 1996).

The number of options available to an innovation system for realization may be as decisive for its survival as the historically already-realized innovations. Although uncertainty features in all innovation processes (Freeman and Soete, 1997), it poses crucial challenges to the governance of innovation especially in the medical context (Consoli et al., 2016; Gelijns et al., 2001), which is the focus of our analyses. Also, the importance of the interplay among *supply*, *demand*, and *technological capabilities* in the medical innovation process is discussed in the framework on the progress of medical knowledge and practice proposed by Nelson et al. (2011) in terms of three enabling forces: advances of scientific understanding of diseases, learning in clinical practices, and advances in technological capabilities (which often originate outside of medicine) for the development of novel modalities of diagnosis and treatment.

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[1] Unlike variance analysis, uncertainty analysis in terms of bits of information does not presume normality in the distributions (Garner and McGill, 1956).