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ScienceDirect
Technological Forecasting & Social Change 75 (2008) 517–538
Technological Forecasting and Social Change

Multi-path mapping for alignment strategies in emerging science and technologies

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Received 28 September 2006; received in revised form 5 July 2007; accepted 1 February 2008

Abstract

Roadmapping serves both short and long term (strategic) alignment in science and technology (S&T). Forecasts of the likely future development of S&T are generated; then research and development (R&D) efforts necessary to realize various goals are backcast. But for new and emerging S&T this trusted principle does not work: the likely products are not articulated yet. A promising approach however is building mapping tools based on underlying patterns and indicators of the dynamics of emergence. This paper discusses, based on a first round application in the field of micro and nanotechnologies for single cell analysis, the methodology of such a new approach. The work is linked to a programme of Future oriented Technology Assessment (FTA) activities coordinated within a European nanotechnology research network.

Our paper addresses well-known lacunae of alignment tools from the viewpoints of the path creation/dependency literatures. We then apply these insights to lab-on-a-chip devices for cell analysis. Dynamics of emerging paths can be used to articulate a future structured in terms of prospective innovation chains and potential paradigms. We demonstrate a plausible variety of paths, which provides a *broader* set of strategic choices. This enables management of expectations and hype by which emerging S&T are characterised, and leads to alignment of actors. Our tool can be applied in strategic management of research and R&D at the level of science-to-industry networks. These are becoming an important element in European S&T policy but will only be successful if ways are found for closing gaps in the innovation chain.
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Keywords: Multi-path mapping; Strategic alignment; Innovation chain; Emerging irreversibilities; Strategy support system; Constructive technology assessment

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doi:10.1016/j.techfore.2008.02.002

1. Lacunae and prospects of assessment and alignment tools for emerging science and technology

For innovation to succeed actor alignment in the form of innovation chains from laboratory to products and applications is necessary. Alignment is easier to achieve where the actors are known, their relationships functioning, regulation is largely unambiguous and the technology field is well understood. This is the case with incremental innovation in established technological paradigms. For new and emerging fields of science and technology (S&T) where architectural (radical) innovations might occur [1], conditions of non-linearity and high technology and market uncertainty are typical [2]. This often leaves actors with the alternative of 'muddling through' and capitalising on fortuitous events until such time that there is a feeling of stabilisation and assessments and forecasts have become more reliable. However, in an age of strategic science and high-investment projects decision makers need to identify possible and promising directions and options and influence technology emergence in advance.

These are challenges for current strategic technology intelligence and forward-looking assessment tools. This is especially the case for the recent European Networks of Excellence and Technology Platforms have to deal with: they have been created around new and emerging S&T and have to develop strategies in the early stages of an emerging situation. Out project is embedded in a particular network of excellence on nanotechnology called Frontiers. Among the central aims of the Frontiers Network-of-Excellence (NoE) programme[1] are

a. the coordination of research activities in the research institutes that comprise the NoE (alignment); and
b. the enabling of interactions between industry in creating and sustaining an innovation chain.

These aims pose tremendous managerial challenges: NoEs have to combine 'vertical' or bottom-up management of a portfolio of research projects with 'horizontal' stimulation of science-to-industry innovation chains. This includes actors outside the network, in the case of nanotechnology, start-ups and SMEs which have a lot at stake in entering such risky innovation chains. Many networks and platforms have dedicated working groups or programmes on foresight, strategic planning and anticipation of societal and ethical hurdles to innovation based on emerging technologies. Frontiers initiated in 2006 one such programme of Future oriented Technology Assessment activities (FTA). FTA is used here as an umbrella term for similar forward-looking and/or interactive characteristics of TA approaches. Another term, with a similar outlook but not limited to technology only, is strategic intelligence (SI)[2] which can be produced in evaluation, foresight, or TA projects and comparative studies of national and regional innovation systems etc.

Activities in the FTA programme focus on designing tools and support systems which allow the Frontiers network to develop strategies for a number of different issues relevant to particular areas within nanotechnologies for the life sciences. Our paper centres on one Frontiers FTA project on the stimulation

[1] The EC 6th Framework Programme Network of Excellence Frontiers is a network of 14 European research institutes, which aim to coordinate activities in enabling nanotechnologies for research in the life sciences. The Technology Assessment Programme is part of the Science to Industry work package and the Ethical and Societal Aspect package, and is led by Douglas K. R. Robinson.

[2] Cf. [29].

of alignment to allow for the creation of innovation chains in the field of micro and nanotechnology. The project has added benefit at two levels:

1. developing recommendations for the Frontiers research network; and
2. exploring strategies for specific actor groups (SMEs and researchers).

At both intra-organizational (department-level) and inter-organizational levels in technology and industry, roadmapping has become a fashionable alignment tool. In general it combines forecasts and business strategies.[3] Ubiquitous as it may be, the advantages (and disadvantages) of roadmapping depend on the context in which it is applied.

There is a wealth of literature focusing on the functions, uses and tools of roadmaps in high-technology companies and MNCs [3–20]. In contrast, analyses of assessment practices of researchers and start-ups (who constitute the larger part of Frontiers) seem rare. These lacunae may be explained with respect to the situation of new and emerging S&T. In exploration and early exploitation of new developments, assessment tools (market forecasts; knowledge of the technology and market drivers) are generally uncertain [9,21,22]. New S&T are not defined by eventual application but characterised by 'generic richness', by linking up with a number of different fields a number of new innovations are enabled [23]. New and emerging S&T are often assessed in terms of their potential to "break through" recognized Frontiers, or "disrupt" existing technology-product linkages [22,24,25] — but this might be affected by hyped expectations. In some MNCs separate roadmaps are developed based on anticipation of multiple future scenarios [13] cf. also [26]. Scientists undertake assessments all the time; these assessments are functioning if not always characterised by breadth of focus (a broader view of the field) and depth of vision (i.e. possible applications in the long term). There is general resistance against linearity towards applications imposed upon research: linearity contradicts the open-endedness and uncertainty of cutting-edge research.[4] From our own involvement in Frontiers and interviews done in conjunction with the work discussed here, we can add that unless start-ups and SMEs are part of networks which are able to commission roadmaps for dissemination among their members[5], they are in a difficult situation to develop or buy roadmaps of the fields they work in.

Literature in the management of innovation, expectations management and sociology-of-technology fields has stressed repeatedly that for assessments during early stages of technological emergence, more 'open-ended', flexible yet effective strategies may be useful. This element of open-endedness has been discussed by Fiedeler et al. [27] and Fleischer et al. [28] and implemented in MANCEF's (proprietary) roadmap[6] [22]. Beyond a diagnosis of the situation and suggestions, few assessment tools seem to have been developed and made available to actors. The FP6-NEST 'ATBEST' project addressed this problem in a workshop with practitioners but at a too general level.[7]

[3] We note in passing that 'roadmaps' in the public sector often seem to be no more than outlooks on the future of a field or sector, using Delphi tools, or the more loosely structured 'prospectives'.

[4] Even though group leaders may use roadmap-type forecasts to organize financial support for their research.

[5] As the Dutch MinacNed consortium did in 2006 with their 'Roadmap Micro/Nanotechnology in Food'; cf http://www.minacned.nl/nl/activiteiten/roadmap_mnt_food_nutrition.php.

[6] MANCEF is the US based Micro and Nanotechnology Commercialization and Education Foundation; cf http://www.mancef.org/.

[7] Cf Rip et al 2005 [30] 'Assessment' and 'alignment' can be used somewhat interchangeably where they refer to tools that help assessing actions on the way to an anticipated future - tools for 'anticipatory coordination' (learning curves of 'disruptive technologies'; 'hype-cycles'; roadmaps). In other contexts it may be useful to differentiate, such as with 'anticipatory tools' (foresight exercises, bibliometric analyses, scenario planning, etc); and tools for portfolio and project management.

The point we make is that technological uncertainty is linked back to the underlying dynamics of the emergence of S&T. These dynamics can be explained by the concept of "socio-technical path" [31,32]: multiple actors follow their own paths-as-strategies towards a future of possible (if competing, or mutually exclusive) paths-as-socio-technical paradigms. Whilst following their paths actors consider a number of factors 'along the road' (which contribute a considerable amount of uncertainty, and demand flexibility). The aggregate outcome of actor strategies is the path-as-paradigm. These different paths at the different levels can be anticipated and mapped to some degree. The resulting maps can support in a very early stage (spinning-off of start-ups; portfolio creation) reflections on what road to take (for actors such as research groups, or start-ups), or which roads to support (for programme managers). A map of paths can be embedded as a central element in a support system to articulate the most robust[8] strategy for research groups, start-ups and programme committees (strategic/strategy support system, SSS). An ongoing strategy support system needs to stay aware of the field, allowing the assessment of whether the current strategy is optimum or a transition is needed to another strategy open to this particular actor.

In the paper we report on the (ongoing) development and application of the 'multi-path mapping' (MPM) toolset. We explore the prospects of MPM, which provides strategic intelligence and would allow reflexive alignment. Specifically, we focus on the stimulation of innovation chains in the field of cell-on-a-chip devices.[9] This field is interesting because perceived products/applications would need a high degree of coordination to enable integration of a large number of technology innovations into a platform which itself could be tailored to various applications. In addition, over the 15 years of research and development into lab-on-a-chip devices, larger industry has been reluctant to invest in stimulating and maintaining a lab-on-a-chip innovation chain. Research and development of the components of lab-on-a-chip continue, however innovations in terms of products are few and far between.

The long term aim is to package MPM as a strategic support system for start-up (and more mature) companies. This system comprises a number of tailorized FTA/SI tools. It is being built around the notion of the 'deployment cycle', which mirrors dynamics underlying technology S-curves: in early stages of technology emergence, the more flexible multi-path mapping is used; in later stages, when the technological, regulatory and business context of the (hopefully) growing start-up/SME has matured, the company can switch towards roadmapping for incremental innovation.

Before delving into the context of lab-on-a-chip for cell analysis we explore what the literature can tell us with regards to insights into emerging path dynamics stemming from sociology of S&T, evolutionary economics and organization studies. After selecting a particular (tailored) model from the menu on offer, we delve into the innovation context by setting the scene for the multi-path mapping exercise. We then present two forms of multi-path mapping undertaken in this project. We close with a discussion and outlook for the multi-path mapping approach.

[8] Robust in the sense that it is informed by knowledge of path dynamics of new and emerging S&T.

[9] Cell-on-a-chip devices are integrated laboratories on a chip (Lab-on-a-chip) dedicated to cell analysis and manipulation. They combine many components and approaches from the macro-scale laboratory equivalent: sample preparation, pre-treatment, analysis, manipulation and removal.

2. Insights from studies of path dynamics and alignment

In more or less stable situations, affordance structures [33] are stabilised which frame possibilities and activities.[10] For new and emerging S&T, many paths are possible and thus speculation is needed. Thus, for developing an FTA relating to paths into the future, knowledge of path dynamics need to be integrated into a process of controlled speculation in combination with other analyses. There is now a substantial (and growing) literature on dynamics of path emergence and stabilisation. Here we can only focus on the main lines of research and highlight relevant notions.

2.1. Insights from the literature into the notion of path

From literature on evolutionary economics, notions of technical change were developed in the context of the firm. In his seminal paper, Dosi [34] argued that technical paradigms direct activities in technology development and thus are both rules that guide heuristics and strategic resources to move further (from the actor perspective).

"Technical paradigms are 'models' and 'patterns' for finding solutions to selected technological problems, based on selected principles derived from natural sciences and on selected material technology (...). A technological paradigm embodies strong prescriptions on the directions of technical change to pursue and those to neglect." (Dosi, 1982, p 152)

In their paper investigating the airplane construction regime, Nelson and Winter [35] argued that when different firms share particular search and development routines, these routines add up to a technological regime. The shared direction of search processes adds up to what they term as a technical trajectory at the sector level: The DC-3 aircraft in the 1930s was the template for over 20 years for innovation in aircraft design around piston powered planes with metal skin and low wings. The potential of these elements was incrementally exploited, improving the engines, enlarging the planes, making them more efficient [35].

In the DC-3 case engineers were singled out as the drivers of the development. In other situations, it may be a continuing product-use combination (cf. the recent trajectory of mobile telephony), or industry structures (such as the energy sector) or strategic games (as with Moore's Law for semiconductors). Van den Belt and Rip [36] extended the Nelson–Winter–Dosi models for the late 19th synthetic dye industry, and in particular the new azo-dyes regime. What came together in the co-construction of a trajectory were, (1) heuristics, (2) an exemplary product, (3) a cultural matrix of expectations, and (4) the drive of a "promise champion". The environment had to change and be re-aligned so as to accommodate to the new trajectory and its promises.

Studies in economic history, organizational dynamics and institution theory have also given rise to the notion of paths. The concept of path dependency was first mentioned by Paul David [37] and later by Brian Arthur [38]. The aim was to explain what microeconomics at the time was unable to do: Why do certain technologies become dominant even though they may be sub-optimal (such as the use of the QWERTY typewriter layout in computer consoles)? Path dependency is a self-reinforcing process beyond the control of the actors involved leading to lock-in. Small events can trigger a technological path that is

[10] Affordance structures suggest directions of action, without determining them. Using the metaphor of landscape, "The affordance structure is in the situation, and frames possibilities for action while not determining them. The metaphor of landscape is useful... why climb over steep mountains, if you can follow a path through a valley (if you know the path is there)?" (Deuten 2003, page 14).

then sustained by "increasing returns". As a result, momentum begins to build up and the path enters into irreversibility. This model argues that a path comes into existence behind the backs of all actors concerned and suggests this may be uncontrollably so.

As opposed to pure path dependency, path creation is a stream of research that remains sensitive to lock-in while modelling emergence on the basis of interactions of actors and their environment. Path creation acknowledges agency in the form of 'mindful deviation' and the mobilising of resources by actors leading to the creation of new paths [39]. Of particular interest for us, are the two main foci of the approach: (1) acknowledging mindful deviation as part of the emerging processes, implying that (2) real-time modulation of processes is possible. This broadens the previous notions of path from lock-in to the co-evolution of interactions of networks of actors with attempts at mindful deviation.[11]

Characteristics of path dependency and path creation are combined in a research line in S&T studies around the notion of socio-technical paths [31,32,41]. This model seeks to conceptualise path dynamics both at the actor and aggregate level (similar to technical paradigms).[12] It was developed as a framework to study emerging alignments and entanglements in the field of nanotechnology, and looks at socio-technical paths as emerging as outcomes of actor alignments within and across multi-levels.[13]

Researchers working with the concept of socio-technical paths have recently taken up the notion of emerging irreversibilities. Increasing alignment and entanglement in the concept of socio-technical paths can be linked to emerging irreversibilities [2,41,44–48]. Emerging irreversibilities are punctuations in the evolution of a technological field, which both guide and drive it. They can be defined as 'socio-technical entanglements which over time enable and constrain alignments and activities of persons, institutions and artifacts. As these entanglements become tighter, options are reduced, facilitating certain paths whilst inhibiting others'.[14] Irreversibilities grow over time, shaping and being shaped by the historical affordance structures which guide path dynamics.

The concept of emerging irreversibilities combines emerging structure (as in path dependency literature) with agency (as in path creation literature) by looking at indicators of alignment and stabilisation in the evolution of affordance structures that guide activities in new and emerging S&T. Thus over time as the S&T field becomes more stabilised, the patchwork of emerging irreversibilities become part of the affordance structure that shapes ongoing dynamics within the socio-technical path. This model has a crucial advantage: by repositioning the notion of path as something that is evolving/emerging in real-time, one can attempt to modulate/steer dynamics towards the more desirable actor arrangements and entanglements.

2.2. The models of path used in this project

For this project we draw on the notion of socio-technical path in its two forms: paths as macro-level paradigms characterised by socio-technical alignments and entanglements; and path as micro-level actor strategies projected towards a future paradigm.

[11] Which can have unintended consequences as Anthony Giddens [40] points out "Merton has provided perhaps the classical discussion of the issue. He points out, entirely correctly, that the study of unintended consequences is fundamental to the sociological enterprise" (Giddens 1984, page 12).

[12] Path creation and path dependence studies are also merged in the Free University of Berlin doctoral programme on organisational paths of the semiconductor consortia [42].

[13] Research becomes doable because of alignment across levels (the lab, institute, or wider world; Fujimura [43]). Similarly, socio-technical paths become "doable" when there is alignment.

[14] This is in keeping with the 'actants' notion as network nodes in Actor-Network Theory [49].

With respect to the first notion a path lies at the domain level. The forward-propelling dynamics of incremental innovation act as a disincentive or even boundary to radical options. Entanglements of socio-technical actors and factors are both causes and effects of these dynamics. Predictions and projections of all sorts can be made (as in roadmaps) — outlining the future path of socio-technical development. In the case of cell-on-a-chip this notion of path can be taken as a projected socio-technical path in the overall field of cell-on-a-chip, where current projections, activities and search heuristics add up to an emerging socio-technical path. We emphasise the "emerging" part to it since a socio-technical path can only occur when there is multiple alignment across and between levels (c.f. Fujimura [43] and Rip and Robinson [32]).

The second notion of path is from the perspective of an actor making decisions, developing strategies and taking action. In this case path is like a business model, a plan to connect the present to the future. In both cases managing for the most desirable path is the goal, be it on the individual actor level (such as an entrepreneur) or on the level of the paradigm (national agencies, international consortia).

3. Setting the scene: lab-on-a-chip devices for cell analysis

The vision of performing laboratory experiments at a micro or even nanoscale was first posed by Terry [50] who linked the idea of integrated microelectronics to the notion of integrated microfluidics for chromatography. The notion of a laboratory on a chip based on integrated microfluidics and micro-devices remained for some time as a general notion in the microfabrication community. In 1990 Manz [51] posed that integrated microfluidics could be harnessed to create complex systems that integrate all necessary analysis steps on one chip, labelled as a Micro Total Analysis System (μTAS). The agenda was set to miniaturise existing laboratory analysis instrumentation and in the early 1990s high expectations were raised about the possibilities of performing (bio)chemical analysis at any lab-on-a-chip and at anytime, for example, total blood analysis at the patient's bedside (Point-of-care testing). In 1993, Harrison and Manz [52] reported on a breakthrough regarding the successful miniaturisation of the analytical technique of capillary electrophoresis, which provided impetus to the field and stimulate a proliferation of research projects towards the vision of μTAS.

In the mid 1990s other scientific communities (synthetic chemists; biologists) were attracted to the field, foreseeing that this technology could aid them in their work or enable new lines of research, such as microscale reactors on chip or experiments with living cells (cellomics). The new and broader notion lab-on-a-chip became widely accepted. Around 2000 nanotechnology started entering this field, offering improvements to existing chip components, but also providing novel concepts for separation and detection, cell analysis, cell manipulation etc.

Also, in the field of biomedical research, off the back of the Human Genome Project[15], a major emphasis in cell biology over the last decade has been focused on in areas related to genomics, proteomics, medical diagnostics, and detection of trace amounts of biological agents. High-throughput screening and microarray technologies are now in common use for measuring gene and protein expression and for assessing biological activity of potential drug targets.

For the field of lab-on-a-chip there is a general agreement of four consecutive phases of technological development (see Fig. 1). Currently most developments still remain in phase 2.

[15] http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml.

Phase 1	Involves R&D in individual processes, instrumentation or devices, such as microfluidic research, pumps, valves, mixers, etc. – elements of an integrated system.
Phase 2	Experimental integration of some of the elements in phase 1 for analysis in the laboratory. These systems are complex and difficult to manage and thus are confined to research laboratories.
Phase 3	Integrated platforms which have refined the experimental integration into a chip sized system which can be incorporated into a device and used by a consumer.
Phase 4	Product tailored for a specific application. This is a customised and packaged lab-on-a-chip based device for analysis or synthesis. Examples could be point-of-care diagnostics of blood samples, or DNA analysis device for crime scene investigations.

Fig. 1. Phases of materialization of the vision of lab-on-a-chip.

This can be translated into a prospective innovation chain diagram (see Fig. 2) where we see scientific and technological research on the left-hand side of the diagram, where ad hoc integrations of a number of the necessary systems for lab-on-a-chip devices are explored and tested as technologies in of themselves as specific capabilities, techniques or devices. Examples could be a microfluidic channel, a fluid mixing system, a sample injector, positioner, sensor etc. In this dotted bubble, researchers attempt to develop and bridge the technology hurdle of integrating these proof-of-principle devices and combine them into an experimental platform for systems research such as protein analysis in the lab (moving from phase 1 to phase 2). Such an integration of a number of devices into an experimental system is usually undertaken in a university laboratory. Such integrated systems are bulky and complicated to handle, operate and maintain, and thus are only suitable for laboratory use. This activity is a bit further down the line from the initial cutting-edge research, and demarcates in many (but not all) laboratory settings the boundary between where research ends, and technology development begins.

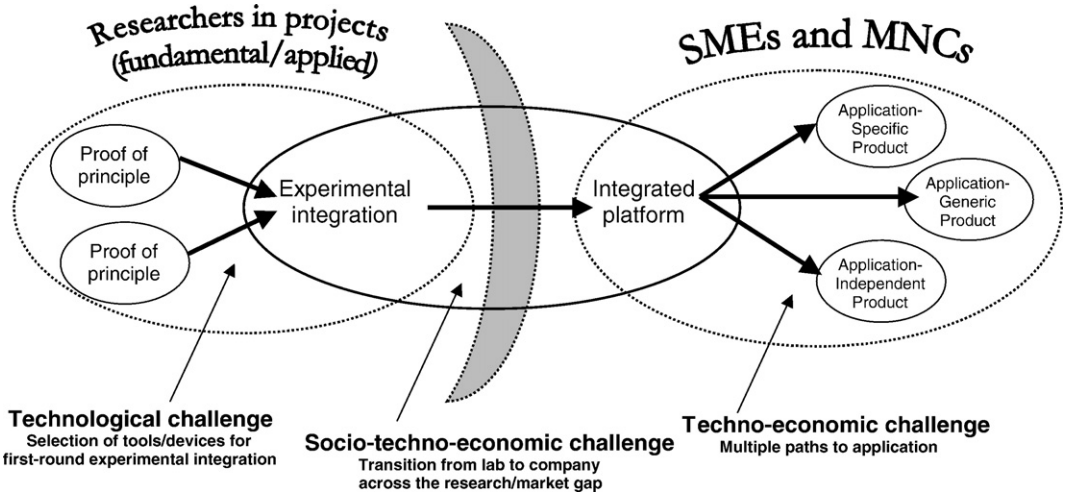

Fig. 2. Broader innovation issues of the transition from research lab to company in the single cell analysis innovation chain.

The central bubble describes the further technical development of an experimental integration of elements into a working lab-on-a-chip device (transition from phase 2 to phase 3). This development is the largest stumbling block over the past years (as described in the history above) since there are a number of routes The decision has to be taken, sooner or later, whether to go for a highly application specific product (one purpose only), a product that is somewhat more generic and would allow for a number of distinct yet still similar operations, or a highly generic, versatile LoC device for many purposes (like a through a plug in and play technology platform).

The grey crescent represents the present barrier which must be crossed in order to produce an integrated lab-on-a-chip device. This barrier will be explored later in the paper as the main gap in the innovation chain for the last 15 years, relegating developments of LoC to remaining in phase 2.

The final large bubble represents the evolution of an integrated platform to a product application. Application driven innovation chains would find that what we term integrated platform and product application being one-and-the-same. However, the various possible prospective innovation chains include the notion of generic integrated platform which can be tailored for specific applications and thus we make the division in the diagram.

For single cell analysis, nanotechnology based tools are beginning to emerge as promising devices for single cell and subcellular analysis. Although current microtechnologies (including microfluidics) provide a foundation for creating a nanotechnology interface with single cells, both the integration of multiple functions and automated analysis and data handling remain to be accomplished in a self-contained cell-on-a-chip. Besides the challenge of integrating many components and devices, a more general challenge is how to bridge technology research with start-ups and/or multi-national corporations to allow technology applications suited to market demands and more broadly, societal needs: Who will be the key actors in stimulating the innovation chain (noting the reluctance of larger industry to stimulate innovation chains) and creating a platform?

With a multitude of projections of technology configurations and possible applications in circulation, and the lack of successful innovation chains meaning lab-on-a-chip remains at the research level, a project was set up under the framework of the Frontiers Technology Assessment Programme to:

1. explore and develop tools to map possible futures for the field of cell-on-a-chip with a focus on single cell analysis and identify possible promising paths for the technology;
2. use analysis of path dynamics and other strategic intelligence to explore the robustness of specific paths located within the field map; and
3. evaluate which paths show the most promise of successfully bridging the gaps in the innovation chain for single cell analysis with lab-on-a-chip technology.

Thus, multi-path mapping necessitates a deeper understanding of path emergence. This is in order to develop a robust map for an emerging situation, but also as part of the ongoing assessments which need to be evaluated based on dynamics of path emergence. In our project we developed multi-path mapping in two ways: (MPM-1) the technical dimension of the MPM was based on desk research as a map to be used for the Frontiers network to aid strategy articulation in research and science-to-industry linkages, and (MPM-2) was used in an interactive way with practitioners as part of a workshop on bridging gaps in the innovation chain from the perspective of practitioners. We fed MPM-1 into the process of developing MPM-2 to combine both field level MPM with practitioner specific MPM. The workshop was used for the co-construction of the organizational dimension of the MPM, where the underlying path dynamics could

be illustrated and discussed. In the following two sections we will describe both MPMs, focusing on their utility.

4. MPM-1: technical dimension

Lab-on-a-chip specifically for cell analysis is particularly relevant for Frontiers research lines due to its focus on instrumentation based on nanotechnologies for the life sciences. Of particular interest is the proliferation of research and development of nanotechnologies for cell analysis the laboratory, the proliferation of expectation of applications for such cell-on-a-chip devices, but no real bridging of the gap between experimental integration and integrated platform (cf. Fig. 2). Thus our first aim with the FTA project was to prospect possible socio-technical paths based on projections of the relevant communities involved in research and the prospected innovation chains. Cell-on-a-chip development is at a very early stage; much of the discussion of cell-on-a-chip development remains at the level of projections and claims.

For Frontiers, the abilities to map possible emerging socio-technical paths and use them to direct the portfolio of research lines within the network would be attractive (management issue 1 — see Section 1). In addition, such a multi-path-map would allow plotting of possible innovation chains and enable the network to constructively stimulate innovation chains stemming from its research choices. Eventually, this allows targeting of research and the negotiation with various relevant innovation chain actors.

For cell-on-a-chip, research areas are based around the perceived functions for cell handling and analysis conducted today in a macro-scale laboratory:

(1) cell culture;
(2) sample treatment;
(3) selection of what you want from the treated sample;
(4) lysis or incubation of the cell;
(5) separation of cell lysate (or single cells); and
(6) Analysis.

Relevant research for instrumentation and approaches for each of these stages is positioned in the proof of principle section (phase 1) of the innovation chain shown in Figs. 1 and 2. Such areas of research have proliferated over the last 10 years [53,54].

Each of these six functions houses scientific research and technology development. We want to point out that within the six functions attributed to a cell-focused laboratory on a chip, research is ongoing with many variations and techniques being attempted or planned within each functional area. Examples for selection of cell would include optical manipulation of cells in microfluidic devices, including the parallel manipulation of cells using optical tweezers [60], optical switching of cells in fluidic channels [59] and patch clamp devices [63]. Recently, microfluidics for cell culture, flow cytometers [58], and other microscale flow-based cell analysis systems have been investigated for cell detection. Microfluidic devices for cell treatment, which includes cell lysis, cell culture and cell electroporation, electrofusion, and optoporation, are also under investigation.

In a number of cases, some of these devices have been integrated into a simple experimental system (cf. Wheeler et al. and the Fluidigm Corporation [55]). This has stimulated hopes for the field of single cell analysis, and promises about tissue engineering on a chip, stem cell analysis and possible production,

single cell based biosensors [61,62] etc., are now being circulated by many of both the μTAS and biology communities. Aside from these relatively simple experimental integrations there is the same gap in the innovation chain which we have diagnosed in Section 3 — a gap in innovation of full experimental integration and evolution into and integrated platform. The visions of lab-on-a-chip devices still remain a promise just out of reach. With many start-ups and SMEs focusing on individual components related to the six functions, there is a sense of urgency in creating a platform for integrating various components into lab-on-a-chip devices for cell (or any) analysis. We come back to this in the next section where we look at specific innovation chains for cell-on-a-chip.

This part of the project was to develop a tool to be able to gauge the ongoing developments articulated related to the possibility of cell-on-a-chip devices. Using literature analysis and a number of semi-structured interviews we constructed a map of the actual and possible technological and application paths for chip-based cell analysis platforms (*cf* Fig. 3). The map indicates that actors can select between two distinct yet general clusters of technological paths within cell analysis: using multiple cells for analysis (MCA), detection, or as 'cell factories', and using single cells (SCA). The former has already been realized to the extent of experimental integration [55,56]. Single cell analysis in itself can be achieved using lysed cells (i.e. cells where the membranes have been intentionally ruptured) or intact cells. Multiple cell analysis is a technology path in as far as platforms and instruments are constructed around the principle of using multiple cells; compared with single cell analysis this has certain advantages and disadvantages in terms of application that need not be discussed here. Any cell analysis technique

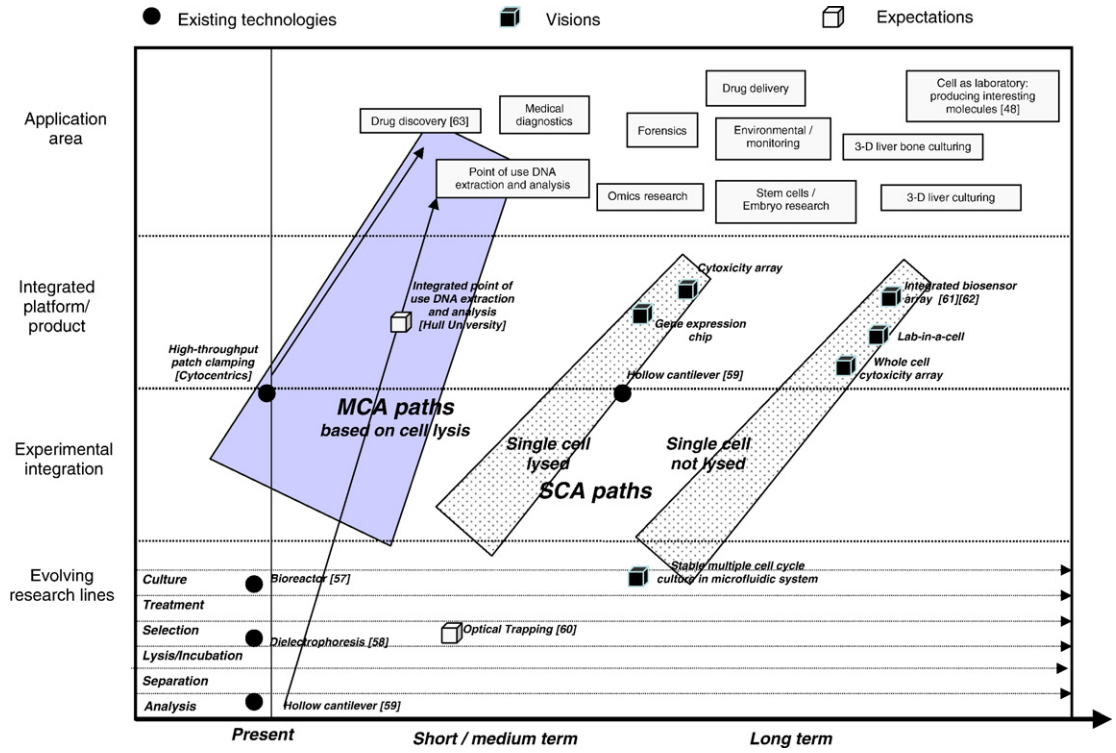

Fig. 3. Technological multi-path map for cell-on-a-chip (Bioreactor [57]).

however can use different approaches and technologies shown in the lowest band on the diagram. Each decision is strategic as it requires investments and expertise on the parts of actors involved which constrain lateral freedom (at a certain point it will be difficult for SMEs to switch to another approach) but propel activities along a trajectory, such as the patch-clamping path [63]. That is why there are always more paths as defined by underlying physical principles within the larger path.

There can be a number of technological paths towards one application area. This is because the labels ('medical diagnostics'; 'drug delivery') are abstract. Nevertheless more defined purposes require more specific technologies and hence, particular technological paths.

The map shows the possible paradigms that can emerge. In the future, drug delivery could be based on socio-technical entanglements created around multiple cell analysis. These entanglements would be based on, and in reverse maintain, the existence of innovation chains around MCA linking actors in research, experimental integration, integration into platforms, and heterogeneous users in drug discovery. To the extent that this path would also comprise benevolent regulation and S&T policies, what we show here as the possible future path/paradigm at the level of an application area (drug discovery) may also be called an innovation system.

The existing technologies and the visions we have mapped here refer to results, or visions, of actors involved in the innovation process. Actors can and do link up with application areas such as those mapped in the top section of the Figure. The Figure also implies that, from a technical point of view, the future path of drug delivery can either be dominated by MCA or SCA. However, it is only the aggregate effect of actors linking up with visions of application, as well as each other, and responding to external events, which redefines an application area as a socio-technical path. In order to really change a paradigmatic path, concerted and sustained interaction of actors in and around the innovation chains is necessary.

The resulting first-round MPM shown in Fig. 3, brings together into the same space:

(1) research projections;
(2) applications;
(3) possible integrated platforms;
(4) possible paths; and
(5) general time axis and stages of innovation chain.

The actual MPM would show many more specific paths plotted within the clusters of MCA and SCA outlined here. We have plotted two actor-strategy paths into the map to illustrate some of the details that can be included in such a map. The first path shows a technology that is already present within a start-up company (as a prospective component of an integrated system) and its own projection of a path where it should go. This path originates at the interface of experimental integration and integrated platform since it is a specific device searching for integration but having been demonstrated as possible within the laboratory (Cytocentrics B.V., Eindhoven). The second path comes from a research project at the University of Hull (UK), where government support has been granted to refine existing technologies and develop an integrated platform for DNA analysis, with a particular focus on point-of-use. This integrated platform has been funded to develop "At scene of crime DNA characterisation" with the aim of demonstrating an integrated platform and then securing funding to turn this into a product for crime scene investigations.[16]

[16] Cf. EPRSC project reference EP/D040930/1.

Such an MPM-1 can be useful for developing a portfolio of research projects and targeting the stimulation of innovation chains. This links up with management challenge 1 for Frontiers: creation and ongoing analysis of a portfolio of relevant research. Innovation chains are specific and there is a lot at stake for those who attempt at creating (or becoming a part of) an innovation chain. Looking at specifics of innovation chains addresses the management challenge 2, development and maintenance of science-to-industry links through stimulation of innovation chains.

For the purpose of aiding development to strategic research area setting within Frontiers, this map (and any future evolution) is and will be integrated in the Frontiers Roadmapping Initiative. The initiative is a programme focusing on aiding research foci in the link to applications. The next step of our project was to focus more intently on the second management issue — that of innovation chains.

5. MPM-2: innovation chain dynamics

Referring to the two management challenges of Frontiers, Section 4 described and explored a use of MPM as support for the articulation and ongoing assessment of Strategic Research Areas based on dynamics of the field as a whole. The second challenge for Frontiers, that of stimulation of relevant innovation chains, is the subject of this section. Whereas MPM-1 was based on the FTA-analyst mapping of the emerging field, MPM for various possible innovation chains requires insights from practitioners who have experience and something at stake in creating and maintaining innovation chains.

To this end, we facilitated a practitioner strategy articulation workshop. The workshop focused on mapping possible innovation chains and challenges for progressing down the number of possible options. The two aims of the workshop were:

1. Developing strategic information for the Frontiers network to include within the framework of MPM-1 in order to direct research and seek out possible actors who could co-construct an innovation chain based on the Strategic Research Areas of Frontiers.
2. Broadening the perspectives of the practitioners participating in the exercise to test the robustness of MPM as part of a strategy support system for prospecting innovation chains.

Building off MPM-1, we conducted interviews based on perspectives and projections of the field of lab-on-a-chip for single cell applications. Along with the MPM-1 it was important to insert details of affordance structures and their co-evolution with emerging irreversibilities, in order to evaluate and assess possible paths within the prospective socio-technical paths. To this end, we used socio-technical scenarios to house some of the more detailed path dynamics and issues that came from interviews and desk research (on socio-technical scenarios in general see Geels [64] and Elzen et al. [65,66]). These scenarios in themselves contained reliable information on the current situation and selected prospective chronologies of innovations in cell-on-a-chip (rather than possible choices to go for). Their purpose was also to prepare participants to the kind of anticipatory work that was one of the workshop's aims.

From the interviews and the work already done on MPM-1 we identified the central bubble in Fig. 2 as the greatest challenge to overcome for cell-on-a-chip (and lab-on-a-chip more generally). As possible participants we identified (1) researchers in microfluidics, microfabrication and nanotechnology tools for cell analysis and (2) start-up companies and small- and medium-sized enterprises (SMEs) relating to specific cell analysis techniques and lab-on-a-chip technology. Fourteen selected practitioners attended the workshop on 12 June 2006 in Amsterdam. Due to the aims and constraints of this paper we have to

describe the details of the workshop process elsewhere.[17] Here we focus on the results relating to the MPM-2.

The group identified a number of existing (or attempts at) innovation chains in the broader microfluidic/cell analysis fields:

- In-house R&D of a multinational corporation (MNC)
- Technology development conducted by SMEs but stimulated by an MNC
- Start-ups finding opportunities and becoming the integrator
- Separate integrators and design houses
- Research device is picked up by someone
- Groups of heterogeneous actors coming together in a cluster

The four options shown in italic where chosen to be discussed in more detail; *cf* Fig. 4. The MPM scaffold allowed organizational challenges and technical challenges to be placed side by side with the goal of prospecting innovation chains. In this case we left the technical steps in the chain as part of the axis whilst the content of the map focused on organizational arrangements and roles of actors at different stages of the chain. We overlaid on top of the chains the challenges and hurdles linked with each chain. On this basis the chains were evaluated.

Within the group there was an agreement that multi-national corporations, such as Siemens or Philips have the capability to undertake research into components and integrate them into a lab-on-a-chip technology platform. Thus innovation chain 1 was said to have a key stumbling block — no clear market is visible for return on investment and thus. Identifying the end user is one clear approach to selecting the components and configurations of a technology innovation chain. However one of the participants described the hedging of bets on a particular end user as dangerous because the innovation chain is precarious and may collapse. Flexibility is attractive for developing sustainable innovation chains but requires a belief in the technology. The participants agreed that this is lacking in MNCs due to previous hype-disappointment cycles — such as in biosensors. Another issue is that cell biology is diverse and so for cell-on-a-chip many niche markets will be the key. Large industry will be unwilling to invest in such niche markets (such is the case in pharmaceutical industry). Perhaps when a generic platform is the target large companies may invest, but application focus for cell-on-a-chip will be niche market oriented.

However, the large risk of little return-on-investment has stimulated another form of innovation chain initiated by MNCs shown in innovation chain 2. This shifts the risk to SMEs which the MNC contracts for risky projects. Thus MNCs attempt at shifting the risk to start-up companies which build on their own ties with the research community and attempt to develop the technology. Intellectual property (IP) is shared with the MNC. Major issues here were agreed in the workshop to relate to the relationship between MNC and start-ups: for example the sustenance of the innovation chain is wholly dependent on the whim of the MNC. Moreover the concern was raised about the protection of IP: although the IP can be shared MNCs have the capability to turn it into a product and defend any IP issues based on their large resource base. One of the participants gave a case example: a large multi-national pharmaceutical company initiated the development of a prototype integrated device for chemical analysis with a number of start-up companies

[17] For some more information on this and other elements of the Frontier FTA programme, contact Douglas K. R. Robinson or go to the programme website: www.technology-assessment.eu.

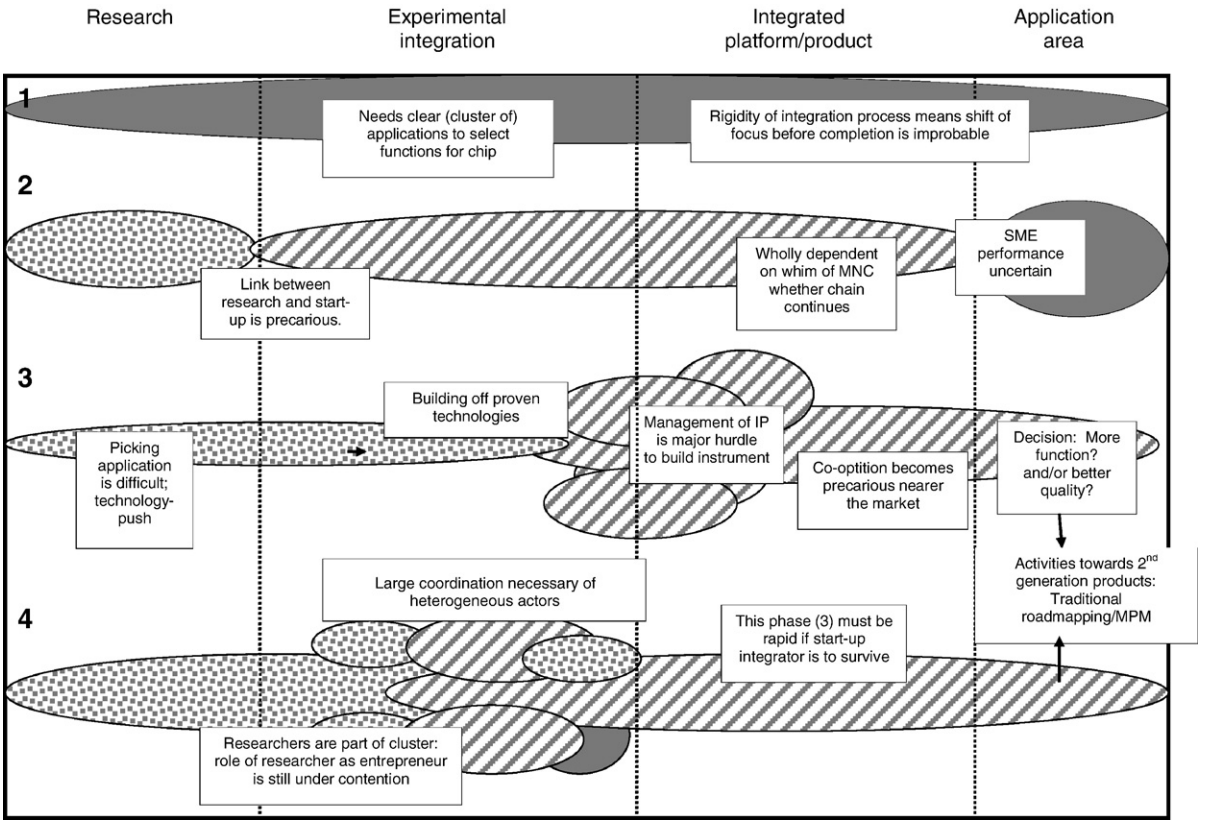

Fig. 4. (1) MNC (dark grey) in-house; (2) SMEs (shaded) chain stimulated by MNC; (3) Start-ups creating network; (4) Heterogeneous clusters.

but then proceeded to outsource the further development of product to another company with the end effect of the start-up companies being dissolved.

Another obstacle came from the MNC perspective based on the risk of outsourcing the development of an integrated platform to SMEs: the performance of the SME is uncertain. The group posed innovation chains 3 and 4 and explored these as ways of bypassing any MNC lack of interest in integration by new forms of innovation chain.

In innovation chain 3 a consortium of start-up companies would be the initiator for bridging the gap by attempting a generic integrated platform which could then be tailored for specific applications. This proposal was based on a view from the Netherlands: here similar SMEs waiting for the integrated platform to arrive are struggling to survive and are motivated to take action. Networks of start-ups and SMEs related to micro and nanotechnology (*cf* MinacNed) already exist. Thus a form of co-option would be the desired goal to take the step of integration together and then competing based on tailored products and added value. The workshop participants agreed that the attractiveness of this innovation chain would be tempered again by IP issues — a large number of companies, distributed IP, difficult to see how each member as well as the collective could capitalise on the developments. The degree of complexity of an integrated lab-on-a-chip platform would mean a clear application driver for the SME-consortium or the

move towards a generic platform in which all would benefit would be needed as a guiding vision. The idea of a generic platform is still contended (this contention was included in one of the three socio-technical scenarios) and thus mobilising the resources to create a generic platform may be tempered by uncertainty of whether generic platform (rather than specific application tailored innovation chains) is the path to take.

An alternative to this path was innovation chain 4 which focused on heterogeneous clusters. Since a large investment is needed in integration, there are specific advantages to be gained by building on proximity relations. This comes from building up capacity based on resources in the region, as well as a funnel for innovations coming from university research. Thus such a heterogeneous cluster would centre around university research and fabrication facilities[18], where start-up companies (and perhaps larger companies) would form the constituents of the heterogeneous cluster. On the one hand, large investment in coordination is necessary and mobilising and coordinating resources is a key issue. On the other hand, advantages of such an approach are that new innovations will be occurring within the cluster, and proximity will allow for knowledge exchange and the building up of trust.

The workshop participants pointed out that there are attempts at all four innovation chains. Innovation chain 1 has been attempted by large companies such as Siemens for relatively simple integrated microfluidics. One participant mentioned a "Lab-cow": an interesting integrated microfluidic device was designed first and then began the search for an application, leading to more loss of confidence in such ventures by MNCs. Innovation chain 2 has occurred with companies such as Glaxo-Smith-Kline[19] and spin-offs such as those University of Hull (UK) and Yole Developpement, a French MEMS business development consultancy.[20] There are attempts in the Netherlands for innovation chain 3 building off micro and nanotechnology SME networks such as MinacNed.[21] Innovation chain 4 is currently occurring at the University of Twente (NL) where a start-up company with a specific sensor is acting as platform integrator.

Each of these innovation chains are possible, but 3 and 4 were agreed to be the most plausible ways forward (based on past failures of innovation chains 1 and 2). The participants also raised more general issues which came up as part of the exploration of innovation chains. A major point was IP for distributed development of an integrated platform, the agreement being that new models need to be sought. For innovation chain 3 this is indeed a challenge. For innovation 4 however this can be handled if there is one system integrator which targets a specific application and builds its network based around this. The IP issue can be generalised to many projected nanotechnology innovations, where technologies cannot be products in themselves but must be part of a system of technologies to be enabled.[22] Furthermore, the workshop participants recognized the difficulty of researchers in public institutions getting credit in developing integrated platforms. Although pressure is on them to provide research that can be turned into innovation chains, there is little acknowledgement of time spent on doing this as opposed to research and teaching.[23] One way of doing this is developing an integrated platform based on an interesting

[18] This agglomeration effect of technology platforms is particularly strong for nanotechnologies [67]. For cell-on-a-chip devices, access to a large number of facilities is needed from microfabrication equipment, to bio labs, to instrumentation such as optical tweezers [60].

[19] Source: workshop participant.

[20] http://www.yole.fr/.

[21] www.minacned.nl.

[22] Examples are targeted drug delivery, implants, sensors etc. enabled through nanotechnology. Exceptions however include coatings and catalysts, which can in themselves be turned into innovations.

[23] This also a general issue in relation to the current situation of strategic science and application oriented research.

experiment. For example, the University of Hull's crime scene forensic device is one case where funding was given to develop a prototype device for DNA analysis, with the added advantage of demonstrating integration possibilities for a cell-on-a-chip device.

The outcome of the workshop was that innovation chain 4 is agreed to be the most promising approach to creating an integrated lab-on-a-chip platform. Salient issues of the management of socio-technical aspects of this particular innovation chain were also highlighted. In the University of Twente case, we see a spin-off company becomes the system integrator for a specific application. In the University of Hull case, we see a research group becomes the systems integrator and builds its network around them with a view to transition to a company after proof of concept.

6. Discussion and outlook for multi-path mapping as strategic intelligence for reflexive alignment

We have reported on a tool to provide ongoing strategic intelligence on evolving actor paths and emerging paradigms related to new and emerging S&T. Its methodological development and shaping owes its robustness to both a study of the relevant literature and interaction with practitioners.

Tools for assessment/alignment have been discussed in bodies of literatures as diverse and heterogeneous as: strategic management of S&T; the strategy literature; the general R&D, innovation management and management literatures; futures studies; organization studies; the S&T policy literature; and bibliometrics, scientometrics, and patent analysis. For the conceptual development of MPM, our self-set task was to integrate insights from roadmapping, dynamics of emerging S&T and expectations, and path dynamics. We argued that for new and emerging S&T path dynamics [68] should be addressed, and can be integrated into FTA activities enhancing the quality of assessment/alignment activities. We mapped initial, potential multiplicity paradigms with path characteristics, as well as the strategies that companies actually use. Shifts of entanglements are possible for actors for some time but otherwise they are more or less constrained as they are caught up in the very path dynamics at strategy and emerging paradigm level observed here. Multi-path mapping allows one to bring technical and organizational perspectives of path emergence and dynamics together in one related space. MPM-1 was developed to map technology-based complexities of future projections from various communities and for various phases of a prospective innovation chain. We tailored this particular MPM with the generally acknowledged phases specific to lab-on-a-chip technology.

The project to which the tool development was linked was characterised by interactions with practitioners around forward-looking discussions. We organized a highly interactive workshop following the premises of Constructive Technology Assessment (CTA) [69], where insights into technology dynamics are explored with actors in order to broaden at an early stage the decision making process. The MPM-2 project involved a collective mapping of projected actor-strategy paths (or actors' paths-into-the-future) and a reflection on the future socio-technical path or entanglements which are foreseen or sought. The multi-path map allows the group to physically map some of the projections, however beneath these projections complex socio-technical arrangements and dynamics – which will enable or constrain some of these actor-strategy paths – could be brought into view. If path creation at the level of application areas is the aggregate outcome of activities at actor levels, then any of the innovation chains identified can create the matrix of entanglements constitutive of the new technology-application paradigm: cell analysis based medical diagnostics could be driven by MNC based innovation, SME based innovation, etc. From the outset

no preference can be given to any chain, even if each of these has its own characteristic challenges to respond to.

Because of the exploratory nature of this first project of Frontiers' FTA programme, we positioned ourselves as experts in the field of S&T dynamics and path creation vis-à-vis the field-level expertise of the workshop participants. For reflexive alignment within research networks or firms it would seem advantageous that a 'strategy support system' (SSS) should be developed as a toolbox to be used without external help. This generic term denotes a toolbox specifically addressing the needs of organizations and networks of organizations with respect to strategic intelligence, possibilities for alignment, and exploitation of the generic richness of new and emerging S&T. The strategy support systems will be further developed for different technology fields being investigated within the framework of the Frontiers research programme. This network level strategy support system is somewhat abstract from specific technological issues, such as cell-on-a-chip; in a way it is a bottom-up way of methodology/tool building, growing with each new FTA exercise at this network level.

MPM can be of use at the level of research group leaders, portfolio managers, and start-up companies. Through analysis of socio-technical scenarios, emerging paths and emerging irreversibilities in the field of research can be anticipated and investigated. Strategic flexibility means different things for different actors and situations, programme managers in particular can use it to be flexible in the selection of projects into a portfolio, monitor them, and over time, reshape the portfolio. MPM helps answering relevant questions such as: What specific kinds of innovation chains can be stimulated? What happens – technologically, organizationally – along the way and needs strategic rethinking? What are upcoming issues for regulation? The maps can be used to train programme officers/portfolio managers on anticipated issues along respective innovation chains, enabling some sort of strategic management including decisions whether to deviate from strategies shown or go along with them.

For a company or specific project leader, the path analysis is with respect to developments in research, the business environment, possible users, as well as regulation. The path they wish to develop strategy for is their company path.

The tool can also be used in communities outside of research and technology development but related to its financing, such as venture capitalists. Here it could act as an anticipation and mapping tool guiding decisions what innovation chain to invest in, or which actor strategies of building up such chains to support. It can be linked with assessments of hype cycles, by contrasting the hype surrounding particular paths with the kinds of path-typical challenges that can be anticipated.

With respect to our tool (but also any other tools developed by social sciences scholars exposed to the research reality) we encourage diffusion into the wider public and private domains. There are numerous examples where research and R&D intelligence is separate from strategic management intelligence embodied in specialized technology consultancies but both cooperate in the context of alignment exercises. For example, there have been numerous Strategic Support Actions (SSA) of the FP6 Thematic Areas that supported roadmap building and where consultancies were involved. Therefore, what would suffice is to articulate a generic SSS sufficiently enough so that consultancies can take it 'off the shelves' of scholarly research and apply it. Such diffusion could be accelerated with support of FP7 Activity Areas.

At the time of writing (March 2007) we can undertake some preliminary impact assessment because the conceptual development and refinement of the MPMs was linked up with an interactive workshop. The workshop participants accepted our diagnosis given in MPM-1 and scenarios as well as the MPM-2 tool as relevant. This allowed discussion to go ahead on forms of innovation chain and ways of bridging

the gaps. Therefore we would claim immediate usability as a positive impact indicator. At the level of Frontiers the tool has been taken up in official documents as MPM-1 was included in the first round strategic planning document known as the Frontiers Roadmap for 2006/2007. This acknowledgement is another positive impact indicator. Further developments of MPM-2 will be included in the following evolutions of the roadmap, however monitoring the affect and further developments of the MPM-1 approach is an ongoing task.

A very concrete impact on strategy articulation comes from one of the participants, a young start-up company initiated in February 2006 with intentions to be the systems integrator of a lab-on-a-chip device focused on a specific application in the medical sector. This start-up company is attempting innovation chain 4 (heterogeneous clusters) based on an application oriented innovation chain where users are already involved in the design process. As a consequence of their use of this tool, they have approached the authors in order to further apply the management tool to see if they can gain extra insights on organizational innovation chains (as well as the technology paths), and thus a tailoring of the tool for the start-up company is currently ongoing.

Acknowledgements

This work was funded through the Technology Assessment Program of the Dutch Nanotechnology Consortium NanoNed – led by Arie Rip (University of Twente) – and we would like to acknowledge his input into an earlier version of this tool. We would like to thank also the practitioners who participated in the workshop. This work was done also under the framework of the Frontiers Technology Assessment Program.

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