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The Politics of the Human Genome Project

Do Institutions Matter?

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The Politics of the Human Genome Project. Do Institutions Matter?

Vittorio Ancarani[1]

ABSTRACT

Literature on knowledge-based economy emphasizes the complex network of actors and sectors – academy, industry and government – taking part in the construction of new science-led technology sectors. Emphasis on horizontal path fails, however, to account for the distinct impact that governmental and political institutions exercise on creating a framework where all the parties cooperate and compete in high-tech fields. From a new-institutionalist perspective, this paper analyzes the Human Genome Project, and finds out that the US government impacted impressively since from the early beginning up to the operational implementation of the project and favored, by means of a property right regime, the emerging of genomic industry.

INTRODUCTION

The recent literature on knowledge economy has emphasized the complex web of interactions between academia, industry and government as the appropriate setting for the development of high-tech sectors. Etzkowitz and Leydersdorff [1997] describe along a triple helix model, and put all the three spheres on an equal footing as both functional and institutional conditions for the knowledge-industries to evolve. By emphasizing the overlap of the three spheres as a driving force of the innovation dynamics, the authors have put a great emphasis on major arrangements between science, economy, and government and have greatly contributed to focus on the way knowledge-led industries are being generated. Further, the triple helix model has made great sense of the economic approach of universities and public research institutes as a strategy aimed at winning their own living and survival. The waning boundaries between academia and industries, an often observed phenomenon which Etzkowitz and Leydersdorff assume to be the first cut evidence of a structural convergence, do not offer an appropriate account of the impact of governmental and political institutions on delivering the framework within which the parties - i.e. academia, industries and governmental agencies - cooperate and compete in the high-tech fields.

By studying the different phases along which the Human Genome Project (Hgp) went through from its first proposal to its operational implementation

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and intersection into the emerging genomic industry, this paper finds that the framework delivered by the US governmental and political institutions impacted impressively on the choices and policies which eventually led to the mapping of human genome in the 2001. The US governmental and political institutions, namely the Congress, put at work a 'detached approach' or an indirect approach to the technology policy backed up with the fragmented setting of its federal-agencies (namely the Department of Energy and the National Institute of Health), and a truly decentralized decision-making process. While favoring adversarial attitudes and confrontational patterns of inter-institutional relations, this approach allows the government to take the role of arbitrator and to act after facts, targeting specific behaviors, and therefore producing a fine-tuned policy. This government-shaped setting is mostly apt to mimicking market place forces as it designs exchange rules for the very heterogeneous, diversified, highly specialized technical competencies required in the sector.

This paper argues that the fragmented and decentralized structures of US political and governmental institutions greatly impacted in the success of the Hgp, in boosting up the new genomic industry. Against the background of the neo-institutionalism [Vogel, 1994; Campbell, Rogers, Hollingsworth and Lindberg (eds.), 1991], the paper finds that this pattern, which features the stronghold of US policy-making, spurred the premises of the new genomic sector.

In the first section, the paper reviews science and technology studies and finds some major failures in actor-network and the triple helix theories and offers an enhanced treatment of the role of state and governmental agencies in the way they impact on high-tech fields. In the second section, the paper analyzes the US political and governmental institutions' receptivity to the Hgp and the policy-making process that shaped the project. After looking at the implementation of the Hgp and its expanding intersection with the bio-tech industry, the paper's third section focuses on two critical episodes in the project life, the first relating to the patentability of genomic information, and the second one relating to the competition between Celera and the public-funded Hgp. In the fourth section, finally, some conclusions are offered.

1. MODELING THE POLITICS OF HIGH-TECH FIELDS.

1.1. Social constructivist approaches.

It has been stressed by many authors that the number of actors who participate in high-tech fields is growing and increasingly heterogeneous [Hamlett, 1992; Gibbons, Limoges, Nowotny, Schwartzman, Scot, and Trow, 1994; Anca-

rani, 1996]. As a consequence, the issue of connecting and coordinating different and sometimes diverging interests and activities among the actors becomes a central one.

This has been for a long time a primary concern in the social constructivists and related approaches in science and technology studies and has dominated the academic mainstream. Drawing on the 'social construction of technology' [Bijker, Hughes and Pinch (eds.), 1987] and 'actor-network' theories [Callon, 1987; Latour, 1987; Law, 1987], students in social studies of science describe high-tech fields in terms of 'socio-technical networks', 'technological systems', or 'innovation networks'. The focus draws on the variety of actors and on the interactions among actors - in some version also objects and technical devices are included as 'actants' - in the process. In this vein, the Hgp has been viewed from some analysts as "entrenched in a highly convergent innovation network, that is, a network in which a scientific, technical and market pole are strongly aligned and coordinated" [Stemerding, 1993: 223-224], from others as a process which "involves assembling an heterogeneous collection of people and objects, without regard for the walls of laboratories" [Balmer, 1996: 532], or even as an "heterogeneous engineering problem of immense proportion" which consist of "building a network of researchers, techniques, organizations, laboratories, databases, biological materials, founding sources, political support, and so on" [Hilgartner, 1995: 305]. According to these perspectives, questions about the nature, success, and duration of a project or a technical field are reformulated in terms of the actors involved, the evolution and strength of their links, and the alliance network and political support sustaining the technology field.

As frequently observed, studies of high-tech fields based on the prevailing social construction/actor-network theories in social studies of science and technology, are committed to an agency-centered approach [Klein and Kleinman, 2002], which often disregards the emergence of power relations and power operations occurring inside the network, and how these relationships affect the evolution of the field [Hard, 1993: 408-416; Wright, 1994: 4-15; Ronit, 1997: 423]. Further, these detailed studies of complex multi-actor networks behind high-tech fields, generally fail – in part because of their methodological premises and micro level focus – to fully take into account the role played by the state in shaping the new fields and their governance regime. For a big project like the Hgp, which since its early stages interacts with government institutions and with an emerging technology sector, it would be thwarting to consider the political dynamics surrounding it simply as a matter of enrolling and linking together allies for the period necessary to fulfill the goals of the program. Inas-

much as they rest widely committed to an agency-centered approach, social constructivists' studies end to flatten to a horizontal sequence of interactions what, instead, occurs inside complex interacting institutional contexts, which define constraints and opportunities for actors, and shape their outcomes[2].

1.2. The triple helix model.

In the stream of literature focusing on the interactions among university, government, and industry, Etzkowitz and Leydesdorff's 'triple helix model' is offering the most convincing theoretical perspective. The model goes quite consciously beyond the 'actor-network' approach with its neglect for the interactions between different institutional sectors. Pointing to the expanding role of the knowledge sector in advanced societies as a major feature of the new knowledge-based economy, they consider the traditional institutional differentiation between university, industry and government as an analytical starting point to which they add a focus on the dynamic forces, interactive operations and communication flows taking place at the interface of those three spheres [Etzkowitz and Leydersdorff, 1997: 155]. This dynamic and interactive perspective goes beyond the 'national innovation system' approach [Lundvall, 1988; Lundvall (ed.), 1992; Nelson (ed.), 1993] and rejects the systemic and quite static analytical emphasis the latter puts on the research system.

Though the 'triple helix' model develops a rich theoretical background which enables to understand the set of challenges and pressures the industrialized and even the new emerging countries face when they engage in the creation of a knowledge-based sector, it has its pitfalls too. In part because the model is built at a very general level, the dynamics occurring in between the three overlapping institutional spheres looks like a driving force, the resulting processes and outcomes of which seem to take place without systematic restrictions or constraints. So, the dominant view conveyed by the model is one of the three spheres all too readily converging together in a process in which previously differentiated institutional sectors tend to become integrated at different levels of structure. This 'convergence bias' incorporated in the model is reflected at the political and policy analysis level, as the two authors look at the policy responses by different countries in term of science, technology and industrial policy [Etzkowitz and Leydersdorff, 1997: 4]. In fact, there is a lack of systematic effort in order to understand different policy responses to similar

[2] For an exception in this literature see Giesecke, 2000.

pressures stemming from triple helix dynamic.

The bias seems to be the consequence of a failure in the 'triple helix' model to give an adequate treatment of the (distinct) role of state institutions in the process. Because of its emphasis on the new innovation environment - which is meant to grow up from the trilateral network occurring among academia, government and industry - the 'triple helix' model fails to offer a satisfying analysis of the impact of political institutions on high-tech fields. In a post-modern mood, the authors equate state and government agencies to other actors; at best the political sphere and the role of government are qualified as one of a 'reflexive' or 'intentional' selector in the resulting triadic partnership. Almost nothing is said, however, about the extent to which political and governmental agencies shape this 'reflexive' exercise. There is not enough analysis of how new issues enter the agenda, which and how many entrants are given authority and influence in the arena, where a policy is being discussed, which and how many centers take final decisions. In a few words, the reflexive exercise should translate in the analysis of the operational performance that state and governmental agencies carry on in order to deal with a big science project.

1.3. The neo-institutionalist approach: the state as a structure and as an actor.

In order to set up a theoretical framework and a research strategy apt to come to terms with the politics and policy challenges raised by the Hgp, a deeper understanding on the role of the government and its performing agencies is needed. The neo-institutionalist literature offers appropriate tools and concepts to address the point [Steinmo, Thelen and Longstreth (eds.), 1992; Lindberg and Campbell, 1991]. State and governmental agencies are being understood in a way that allows charting better its continuing interaction with the economy and the research sector in the high-tech fields, without falling, however, in the trap of assigning all major outcomes to state powerhouse. In a move to understand the role of state in the constitution of an economic sector, Lindberg and Campbell [1991: 375] distinguish "the state as an actor (or an ensemble of actors) and the state as a political-institutional structure". Similarly, Vogel [1996: 20] argues that "to understand the role of state institutions, we must first recognize that states are both 'actors' and 'structures'". Hence – it has been concluded - the analyst has to investigate "how state actions (or inactions) and state institutional forms may condition or structure the strategic choices and power positions" of actors in a given economic sector [Lindbergh and Campbell 1991: 361].

The officials and state agencies responsible for science, the Congress, the President, the Courts and various regulatory bodies, should be considered as ac-

tors entering together with scientists, corporations and other private agents in the process affecting the way the genome field is being structured. They all have got ideas, preferences, and goals of their own as far as the new field is concerned. Further, they have beliefs about the appropriate role, scope, and method of state intervention in the sector. As a structure, the organization of the state in this sector defines the type of relationship between the state institutions and agencies with the relevant high-tech sector. The institutional features shape the preferences, structure the relative power among groups, and play a critical role in guiding the decisional process in the field. Taking the whole set of actors and structures together forms what Vogel [1994: 60] calls a *sectorial regime* (see also Ancarani, 1999).

2. The Human Genome Project.

2.1. The beginning.

The origin of the Hgp dates back to 1985, five years before its official launching in October 1990[3]. This period can be called the initiation stage, or the promotion phase in the project life. The project was not started by an individual administration but by a variety of political entrepreneurs. The idea of charting the complete nucleotide sequence of the human genome emerged in the United States among some powerful members of the scientific community (Roberto Dulbecco, Walter Gilbert), high academic scientists-administrators (Robert Sinsheimer) and officials in federal agencies (Charles DeLisi). First discussed in "small gathering scattered across the country" [Lewin, 1986a: 1598], the proposal was later debated in wider scientific forums and conferences, and took gradually form through the bureaucratic and policy process as well. The media were involved from its very beginning and a talk in a meeting convened by the Italian embassy in Washington by a Nobel laureate, firstly introduced the idea in the international arena[4].

However, for almost two years the project was mainly a matter of few scientists and science administrators. To materialize it had to win the support of the majority of concerned scientists, to avoid disruptive conflicts among the agencies competing to play the leading managerial role in the project, and to

[3] An extended insider account of the first phase of the Hgp can be found in Cook-Degan, 1994.

[4] Nobelist Renato Dulbecco's speech on Columbus day 1985. Dulbecco later became the leader of the Italian Genome Program.

appropriate the necessary funds from the Congress. In other words, proponents had to built a "working consensus and engage in coalition building" to get the project started [Lambright, 1994: 48][5]. As the Hgp was clearly a long term initiative, in order to endure as a stable social and political construction until all the goals were achieved, the supporting coalition needed to be sustained and re-set along the different stages of the life of the project.

2.2. The Doe initiative.

The unexpected place where the project first entered the policy agenda was at the Department of Energy (Doe) as a move of DeLisi, director of one of its divisions: the Office of Health and Environmental Research (Oher). Even if this initiative was rooted in an old tradition of intramural genetic research in heritable mutations, and in the ability of the agency in managing big projects endowed of large capital and sophisticated technology, the move was perceived as audacious and largely motivated by the need to reshape the mission of Doe laboratories in the vanishing of the Cold War. Political constraints on the financial budget, and a legitimacy crisis of what was primarily a defense oriented policy mission as well, pushed the agency to identify civilian applications of its research programs. Introducing a Human Genome Initiative as a new R&D program was seen by science administrators and scientists at Doe as a way to overcome a critical moment in the life of national laboratories and by critics as "Doe's program for unemployed bomb-makers"[6].

DeLisi quickly pushed the new initiative. He started by asking advice in an informal way to the group of biologists working at Los Alamos National Laboratories, and asking support at the agency's highest level. After getting the green light from the Doe administration, he started pursuing the project very aggressively and casted off a first start-up spending for human genome research, setting up consensus in the scientific community and in the Congress as well. A scientific advisory committee was established at Doe with the task of pursuing the internal review of the project and helping future decisions and funding research proposals.

In a workshop at Los Alamos Laboratories in Santa Fe, March 1986, Doe's initiative was discussed for the first time in a larger scientific audience. DeLisi

[5] On coalition building in science and technology see also Hamlett, 1992.

[6] David Botstein, quoted in Cook-Degan, 1994: 188.

proposed establishing two genome Centers at two national laboratories[7], and announced that a first limited funding was provided to get the project started. According to a scientist and Doe official, the initiative received the "near unanimous enthusiasm" of the fifty participants at the meeting[8]. In January 1987 a second meeting in Santa Fe was convened to detail the initiative. The Doe program stressed a five year initial phase focused on physical mapping, improvement of mapping and sequencing technologies, and development of computer analysis tools enabling the enactment of a second phase centered on sequencing the whole human genome. In April, a subcommittee of Doe's Health and Environmental Research Advisory Committee (Herac) released a report which strongly endorsed a fully fledged mapping and sequencing program, urged Doe for a strong commitment in the initiative, and recommended a budget of 40 million dollars for fiscal year 1989 to be stabilized over a five year period at a level of 200 million dollars per year. The report also strongly supported the Doe leadership in the initiative. Even if the need for cooperation among agencies and organizations, both domestically and internationally, was stressed on, yet the report asserted that Doe should not delay implementation of its plan or defer to some other organizations [Palca, 1987: 429].

Up to this point the Doe initiative was clearly at the center stage of the Hgp debate. However, the efforts to build a strong project coalition around Doe as the developer and administrative leader, proved at best fragile. Doe failed a critical step in its strategy: winning support by the majority of the research community. As the Doe initiative set to grow, a great deal of opposition mounted in the academic biomedical community. In its advocacy of a genome initiative, Doe had got some strengths and some weaknesses as well. Apart from being the first promoter of the Hgp, its strength located in experience in managing large scale multidisciplinary scientific and technological projects inside its national laboratories. Doe's commitment in developing new technologies for sequencing and physical mapping as well as in increasing computer capabilities and managing resources such as the gene library project and GenBank - the US database for Dna sequences in Los Alamos – was also widely recognized. Yet

[7] The two Centers, at Los Alamos and at Lawrence Berkeley National Laboratories, were established by the Secretary of Energy John Herrington in September 1987. Another Center was established in July 1990 at Lawrence Livermore by the Secretary of Energy James Watkins.

[8] David Smith, quoted in Lewin, 1986a: 1599.

Doe was removed from the large scientific and biomedical community orbiting around the National Institute of Health (Nih), and felt to partake a different, more bureaucratic, scientific culture from their own. No matter what the merit or substance of the initiative, the bold move ahead of Doe was interpreted in the biomedical research community as a will to proceed unilaterally in a pre-emptive move to the exclusion of more qualified others. Even the rhetoric of technological strength and megascience, put forth by Doe administrative leadership – the project was equated to a space program - proved controversial. This comparison instigated the Big science vs. Little science debate against Hgp, provoking fears that the new initiative would squeeze the funds of other biological areas and eventually transform the social setting and way biological science was to be done.

2.3. The Project under strain (1986-1989).

A harsh controversy erupted in June 1986, when a large group of molecular biologists and geneticists met at a symposium in Cold Spring Harbor. Some eminent scientists gathered there - among whom Walter Gilbert, James Watson and Paul Berg - strongly supported the initiative, though a few of them openly questioned the leading role of Doe in the project. However the humor of the majority, especially among the junior scientists, was clearly against the initiative. A few weeks later, Watson, the future project leader, summarizing the mood of the meeting over the proposal to sequence the human genome, reportedly said that "everyone else at Cold Spring Harbor was against it". Those people were young, he explained. "They are scared that if sequencing goes ahead there will be fewer funds available for their research" [Lewin, 1986b: 620]. Fear mounted in the biomedical community that a mega-scale project of around 3 billion dollars would divert resources from research in other fields of molecular biology, and that a targeted big-science approach to sequence the whole human genome would endanger investigator-initiated research, changing the very nature of the biological research. As a participant put it: "We could embark on a space-lab scale project. But what we've been good at is devising new methods and techniques in small-scale projects. Most of the best development of techniques in biological science has been adventitious, not goal directed. […] The structures necessary to cope with the expenditure of 2 billion dollars could be inimical for biology. It could create immovable structures"[9].

[9] Eric Lander, quoted in Lewin, 1986a: 1600.

Molecular biologists were approaching a sea change in their research environment, in part because of the Hgp, but they were simply not prepared to "a paradigm shifting of molecular biology"[10]. If that change would occur anyway Nih, the university biomedical researchers' reference agency, not Doe with its constituency in the national laboratories, should direct the process.

2.4. Reshaping the project and the Nrc Committee.

The June 1986 Cold Spring Harbor meeting traced a major turning point in the genesis of Hgp. Even if the debate was harsh and significant reservations emerged on the initiative, which at first glance seemed a step back, in retrospect it revealed it to be the beginning of "a subtle but important transition" in redefining the long-term scientific strategy and extending the political support base to the project [Cook-Degan, 1994: 183]. Hereafter, the wider biomedical research community entered the process and a proactive scientific leadership emerged that took a major role in setting the priorities and articulation of the program and in reaching a working consensus inside the scientific community. This leadership acted strategically in a delicate moment in the administrative and political decision making process. At this time a strong entrenchment of the project in the governmental bureaucracy and in the budgetary mechanism was still lacking, and scientific criticisms or inter-agency conflicts could have killed the project at its very beginning.

The reshaping of the project's goals in this opening phase was not simply a technical achievement, "a normal scientific reformulation of the sequencing idea as it met with the needs of a more realistic goal-setting" in the words of Dulbecco [Cook-Degan, 1994: 115]. It was part and parcel of a process of coalition building and negotiations, inside and outside the scientific community, which changed the original aims and scope of the project. This redefinition made it possible for a larger number of actors to be actively involved and, at the same time, to avoid more fractious conflicts and controversies damaging or even preventing the very life of the project. The redefinition/aggregation process took place within the relevant governmental agencies, representatives of research institutions and disciplines, and inside the scientific élite through *ad hoc* panels, and informal groups. However, the main institutional locus in which the scientific review of the genome project formally occurred was at the National Research Council (Nrc), the advisory council of the National Academy of Sci-

[10] Walter Gilbert, quoted in Roberts, 1990: 757.

ences (Nas), the higher representative body of the US scientific community. In September 1986, the Nrc set up a committee, directed by Bruce Alberts, in which to assess the pros and cons of a genome project. The Alberts Committee included at its heights fifteen representatives of the diverse interests and views in the biomedical community. Since in the review process the opinions soon shifted in favor of the project, the committee focused, and proved to be quite effective, in reshaping the scientific strategy and finding an agreement on priorities and goals in genome research. The committee took a wider scientific perspective than Doe. Emphasis on sequencing – the original idea of the first proponents like Dulbecco, Gilbert and Sinsheimer – was dropped.

Even if what Gilbert called the "grail of human genetics" remained the "ultimate goal" of the project, the Nrc report released in February 1988 charted a different progression in the research agenda. Priorities shifted and new goals were added to the initial proposal. In the committee's proposal the first step would focus on the construction of both genetic linkage and physical maps of the genome. Then efforts will shift to sequencing regions of interest of human genome, but also of other small genomes such as bacteria, yeast, nematodes, and the fruit fly. By comprising genomic research of other organisms, importance was given to comparative genetics and interpretation of the human genome. The massive sequencing effort was deferred "until technical improvements make this effort appropriate". This was to mean until innovation in automated sequencing technologies would turn faster and cheaper.

The recommendation of the Nrc/Nsa Albert Committee charted not a monolithic goal-directed project, but a more flexible and pluralistic approach which made possible the inclusion of other areas of biological research. In this way, the project was crafted so as to exercise - as Mainard Olson, one of the leading figures in the committee, told - "a profound impact on all of biology" [Lewin, 1988: 602]. The larger biological context in which the project was eventually cast made it possible to reach a wide consensus in the committee and in the different sectors and research interests of the biological community. The original narrow and targeted strategy gave way to a broad and diffuse approach conducive to building up a wider consensus and mobilizing support in a larger scale.

The revised approach also took a rather different organizational and technological rhetoric then that associated with big science which translated the discursive constellations of big science into the jargon of networking and coordination. In a hearing before a House Committee, only a few days after the release of the Nrc report, when asked about the analogy between the Hgp and the

"so called big science programs like superconducting super collider", Alberts replied: "this is not a big project, anything like that. […] I like to think of the development of computers. The Silicon Valley model is what we're aiming for. We're aiming for a bunch of small, modest-sized groups competing with each other to find the best technologies. After the technologies are discovered, perhaps in 10 or 15 years, at that point we'll be dealing with something completely different, perhaps more analogous to the collider kind of thing. But at the moment, we're not talking about anything like that. I don't see this as a big science project. It's a coordinated series of little science projects" [US House of Representatives, 1988: 34].

2.5. The Nih leadership.

While in the fragmented landscape of US research agencies the Doe's initiative pushed the Nih into the game to defend its global leadership in biomedical research, it was the revised approach delineated by the Albert Committee which made it easier for the Nih to enter more actively in the project without fear of loosing contact with the large constituency of its clients: the individual researchers receiving grants from its National Institute of General Medical Sciences (Nigms), fearful that resources given to sequencing the human genome could threat other research activities. Initially the Nih took a cautious, if not a cool, attitude toward the project. As the major funding source and home of most basic research for life sciences and biomedical research in US, including genetic research, Nih seemed the proper governmental agency to promote and lead a Hgp. However, in contrast to a very committed Doe, Nih seemed very much "the reluctant bride, unenthusiastic about an all-out effort yet unwilling to turn the project over the Doe" [Roberts, 1987b: 487]. In other words, as stated by a participant, the genome project "would require a change in Nih's philosophical outlook and in approaching to research funding"[11]. Stressing on a more phased approach and postponing any massive sequencing effort, devising an enlarged spectrum of research goals, fostering a peer reviewed assessment of research founding, and with an organizational emphasis on networking a plurality of research groups rather than focusing on big genome centers, the Nrc plan was structured in a way more akin to the tradition of the agency.

In fact the élite scientists gathered in the Albert Committee acted as a

[11] George Cahill of the Howard Hughes Medical Institute, as reported in Roberts, 1987b: 487.

policymaking body, helping to reframe the Hgp along a new equilibrium point more in the mainstream of the biological research and its organizational parameters. This move also reshaped the role of actors and institutions in the new policy field. After the release of the Nrc report in February 1988, finally the major biomedical agency seemed fully committed to the project, gradually taking its place, so that it that increased its political share in the new genomic policy[12].

Yet the hesitations and late involvement of the Nih generated interagency tensions and exasperated the issue of the leading agency and project management. In the Nih report the section on the management of the project was the weaker one, partly reflecting uncertainties on the Nih role. Unable to reach a converging conclusion, in the section *Managing a Human Genome Project*, the Nrc Committee put forward three possible organizational options. The first one gave full responsibility for the project to a single agency (however without indicating *which* agency - the Doe or Nih - should play the leading role). In the second option, the central organizing responsibility was placed in an Interagency Committee including representatives of the Nih and Doe and other federal agencies. The third option supported the same Interagency Committee, but suggested that a single agency should be given the full responsibility for handling administration. In all three cases – according to the Nrc report - the administrative bodies were to be assisted by a strong scientific Advisory Board, chaired by "a full-time chairman who is a distinguished scientists", with a prominent role in the 'peer review' process and in the coordination and oversight of the project. As recognized in the report, the role anticipated for the Board "is somewhat stronger than that of a typical scientific advisory board", signaling the prominent role scientist intended to play in the direction of the project [National Research Council, 1988][13].

In the wake of the Nrc report, the way the Hgp should be administered became a hot topic, one able to interrupt the relative insulation from political conflict until then enjoyed by the Hgp. At this stage in the project life, without a strong institutional footing and budget entrenchment, any administrative infighting could have compromised the political support in the Congress. At the

[12] The turning point occurred at the Reston meeting (Virginia), February 29 to March 1, 1988. See: Cook-Degan, 1994: 166.

[13] For comments on the Nrc report, see: Roberts [1988: 725-726], and Palca [1988a: 467].

end of April 1988, the congressional Office of Technology Assessment (Ota) released a report on the Hgp which approached the issue of interagency coordination [US Congress, 1988][14]. The report notes that the Congress could decide for a single agency to carry on the project. It also recognizes the advantages of a leading agency and that the Nih "is the natural choice" for that role. Yet the report stresses quite clearly that different agencies were already involved in the project and that the choice of a single agency "would delay the progress and diminishing overall funding". For these reasons Ota strongly endorsed the creation of an interagency task force entrusted to coordinate the established activities at Nih and Doe.

This more realistic approach, in the form of an interagency committee, eventually was the winning one. The fear of congressional intrusion and legislation on interagency coordination pushed Nih and Doe to sort out their rivalry and to get together and reach a suitable agreement for a coordinating plan. Paving the way for coordination, a Memorandum of Understandings was signed in the fall of 1988 by the two agencies, and a joint subcommittee drown from the relevant advisory committee from each agency was established "to assist the two agencies with programs oversight and coordination"[15]. However, as it was clear from the beginning to the Nih director J. Wyngaarden, what ultimately determined the leading role among the two agencies was less the administrative or coordinating mechanisms than the funding levels appropriated in the Congress[16]. In fiscal year 1990 – the last year before the official beginning of the project – the levels of the budgets were 58.5 and 26 million dollars for Nih and Doe respectively, which gave Nih a *de facto* leadership. The second big gain Wyngaarden was able to achieve in building a strong Nih leading role in the project was by appointing Jim Watson as head of the new Nih genome office. As put forth by an insider observer, "by appointing Watson, Wyngaarden made Nih the center of power in genome politics and harnessed one of the dominant

[14] For comments on the Ota report, see: Lewin [1988: 602-603], and Palca [1888b: 769].

[15] See: Statement of D. Galas, Associate Director, Office of Health and Environmental Research at Doe before the US Senate - Committee on Energy and Natural Resources, Subcommittee on Energy Research and Development , July 11, 1990 [US Senate, 1990: 44].

[16] See: Testimony of James Wyngaarden, Hearing before the Subcommittee on Oversight and Investigations of the Committee on Energy and Commerce - House of Representatives, April 27, 1988 [US House of Representatives, 1988: 124].

talents in molecular biology" [Cook-Degan, 1994: 161].

2.6. Launching the Project.

As the end of 1988 approached, the élite of molecular scientists had secured some major result in building the basic blocks of a pro-genome coalition.

A strong scientific leader at the helm of the project, able to overcome uncertainties about management roles avoiding administrative wars between Nih and Doe.

The Nih, their favorite agency, became the core of the effort, yet in the framework of an institutional partnership with Doe.

A year later, October 1989, in a process of consolidating his footing in Nih bureaucracy, the Office for human genome research became the National Center for Human Genome Research with Watson appointed as director.

The scientific strategy of the project was entirely reworked not only in a technically more persuasive shape, but also in a way conducive to a broader acceptance in the biomedical community.

In 1990, the project faced a final attack of its critics which reached its climax at mid July, when a hearing before the Committee on Energy and Natural Resources in the Senate resulted in a defeat of the project's opponents. The critical statement made by M. Rechsteiner (Utah University) and B. Davis (Harvard), who reiterated their aversion to see too many resources ear-marked to a long-term project, were offset by the heads of the three national laboratories involved in human genome research. The latter offered the results made by the laboratories and university affiliated researchers and announced the opening of a third Genome Center at Livermore's National Laboratory. The announcement by the president and chief executive officer of Genentech, the US largest and oldest biotechnology company, of his "100 percent support" to the effort and the opening statement made by Dominici, a senator from New Mexico and a sponsor of Doe's Los Alamos National Laboratories located there, removed any remaining doubts on how broad based was the support for the human genome project[17].

[17] He announced that "a number of research groups and eminent scientists" had written to him letters supporting the project and that in a pool conducted of over 105 companies by the Industrial Research Institute, the human genome initiative was ranked as number one over other large scale federal projects. He also remembered how the project was evaluated and endorsed by two major reports issued by the Nas and Ota

At the closure of hearing, B. Davis retreated with an accommodating statement: " I would not want it to appear on the record that I am opposing the program. I have questioned how its scale should be evaluated relative to the scale of other biomedical research […]. But I stated plainly that every one of the goals of this project is something about which I am enthusiastic" [US Senate, 1990: 133]. The project's supporters had clearly won the case. Not only a complex and manifold research machine was running, but powerful allies across the public and the private sectors forged strong ties making it difficult for opponents to stop the project.

3. The dynamics of US policy-making. Building intellectual property rights and governance mechanisms in the genomic field.

As the Hgp entered its implementation phase and began to release a growing stream of map and sequence data, genomic research started to attract private financial investment and the interactions between research and industry began to upsurge. As it has been heeded by an inside observer, whereas in the Spring of 1987 Walter Gilbert found insurmountable obstacles to finding venture capitals to start its Genome Corporation, in September 1990 a symposium devoted to solicit interest among pharmaceutical companies, organized by Craig Venter and Gilbert himself, "drew a respectable audience", and in 1992-1993 "private corporate investment in genome research became fashionable" [Cook-Degan, 1994: 345].

After more than ten years from the beginning of the project, and only few months after the joint Clinton-Blair declaration (26 June 2000), in which they announced the completion of the first draft of the human genetic code, genomics seems clearly well rooted in the pharmaceutical business. A new generation of small biotech companies "has sprung up on the back of this scientific breakthrough in genomics or in related areas", mostly with the direct involvement of top academic scientists [Dyer, 2001: I]. They apply novel technologies to "intercept molecular messages, transduce them into electrical signals, capture them on computer systems, analyze them with computer programs, and communicate the results with pictures and words" [Zweiger, 2001: 166] and they can do that with large amount of biological information simultaneously. At the other end of

and, last but not least, enjoyed the support of the President and his scientific advisor Dr. D.A. Bromley.

the industry spectrum, the big pharmaceutical companies are eager to harness the fruits of genomics and of the related emerging technologies both forging alliances with small genomic companies and through their own dedicated subunits and in house programs.

As many observers recognize, genomics and related technologies represent a major change in the biomedical research and in biotechnology and biomedical industry as well. This brought on a remarkable shift in the division of labor among universities, industry, and the federal government in genomics and in the related commercial fields of pharmaceuticals and biotechnology [Powell and Owen-Smith, 1998].

In order to work the new way, the sector needs not only to assemble more and more heterogeneous and highly specialized knowledge resources and technical competences across organizational sources and institutional settings in the public and the private domain as well; now an appropriate governance mechanism[18] is needed, to design reliable property rules for the new knowledge-led sector. As a consequence, in order to regulate the distributional problems [Lindbergh and Campbell 1991: 363], an intellectual property right regime was to be set, "to better fit the emerging need to stimulate production and distribution of information and knowledge" [Granstrand, 2000: 1075].

The analysis of the new sector cannot be limited to technological and economic changes. The property rights regime defined by state and public institutions comes out to be pivotal to the sector's progress. Though stressing on the interplay between university-industry-government, the triple helix model fails to spot the provisions delivered by the government and policy makers. Shaping a property rights regime, the US administration did secure the participating parties a way out to settle distributional issues. In its very absence, the explosive pace of the sector growth, shown in speeding up information resources spun-off from the public funded initiative and, later, from the private sector as well,

[18] Property rights policies are central to understand the transformation of the governance regime of an industrial sector as they specify the relationships of exchange of basic resources among actors [North, 1981]. A property right regime can be defined as the rules and laws that establish the conditions of control of the resources, means of production, and outputs - including physical goods and intangible assets such as knowledge -, also define the power relations in an industrial sector. As a result, struggles and efforts to redefine property rights are chief strategic issues for actors pushing for a governance transformation [Caporaso, 1989: 143; Lindberg and Campbell, 1991: 361-63].

would have triggered uncertainty about property rights and worsened terms of exchange of valuable genetic information.

3.1. The US policy-making and the issue of property rights.

In the 80s, the US technology policy undertook a major turn in the wake of Japanese challenge. A major objective was to enhance technological transfer from science based research institutions to industrial sector. However, especially during the Reagan administration, these changes in science and technology do not translated in an interventionist agenda. The new policy avoided what was seen as an unnecessary intrusion into the activity of private business promoting cooperation across institutional sectors (university, industry and public agencies) by resorting to indirect means through tax and patenting reform. In 1981, the Economic Recovery Tax Act provided substantial tax credits for R&D as well as incentives for new capital investments. Later in 1982, the Department of Commerce encouraged the use of tax shelters for joint R&D ventures [Wright, 1994: 57-58].

The shift was also evident in major changes in patents policy and practice. Firstly there was a clear trend toward an *expansion of the realm of patentability* to new technological areas. These changes "were not brought about primarily by Congressional action, but rather by the re-invigorated patent office which has taken a serious and fairly narrow Court decisions regarding new subject matter and generally interpreted them quite broadly" [Jaffe, 2000: 535][19].

Secondly, there was an *expansion of the subjects entitled to retain rights to patents* stemming from federally funded research.

The Bayh-Dole Act of 1980 allowed universities, small business and government operated laboratories - such as the Nih -, to retain title for invention stemming from federally funded research. A series of Technology Transfer Acts, starting with the Stevenson-Wydler Act of 1980, established the legal and administrative mechanisms for transfers between public (especially the national laboratories) and private entities. For example, the Federal Technology Transfer Act of 1986 authorized the national laboratories to enter into Cooperative Re-

[19] In 1980 for the first time the US Supreme Court ruled that a living organism, a bacterium genetically engineered to clean oil spills, could be patented. In 1988 the Harvard University was allowed a patent to a genetically altered strain of mice. In 1991, a federal court of appeals assured broad protection to a particular gene sequence, the erythropoietin gene.

search and Development Agreements (Crada) as a mean to address industry's competitiveness problems [Branscomb, 1993: 104; Jaffe, 2000: 534-535; Slaughter and Leslie, 1997: 45-46].

Prior to the Bay-Dole Act, universities were allowed to secure property rights only on a case by case basis by federal agencies funding research through a bulky and lengthy process [Slaughter and Rhoades, 1996: 318]. Agencies adopted different policy on this matter, some of them routinely allowing universities to secure patent rights and some rarely or never allowing that possibility [Jaffe, 2000: 534].

The new legislation, while explicitly making clear that technology transfer to the private sector was a desired effect of federally funded research, reduced administrative leverage and discretion to the commercialization of research. The new intellectual property right (Ipr) legislation sought clearly to instigate public and private agents to pursue an innovation policy avoiding any direct intervention on the organization and coordination of the new rising high-tech research sector. Etzkowitz and Gulbrandsen [1999] have noticed the point, though, featuring it more as the mark of a long lasting *laissez-faire*, anti-interventionist ideology. For them, the indirect and decentralized approach of the US policy-making is an 'elaborate subterfuge' or a simple transitional step toward an European-style interventionist approach to innovation policy.

Quite the opposite is the contention of this paper. The US policy-making reflects not only an ideal preference, inspired by a new wave of supply-side economics; it is especially affected by its institutional landscape, which deserves to be discussed on its own right. Indeed, the US policy-makers do not regard government intervention in technology and innovation policy as legitimate, though they can endorse it when a specific rationale is attached. What make the difference are the fragmented and decentralized institutions of American policy-making. The latter and not so much ideal preference keeps the government to act in a proactive way. Rather, what emerges in our case is an indirect and decentralized innovation policy pattern, which clearly contrasts with the more direct interventionist approach usually found in Europe.

3.2. The Ests controversy.

A major concern about the patenting of data and the potential threat to the open exchange of information surfaced from the very beginning [Roberts, 1987a]. As the project began unfolding, the topic of patent protection took a central stage in the US genome politics.

What was unexpected to many was how early and where the patent route

was taken from. The move that caused the beginning of an enduring controversy over ownership and control of genome information was the Nih decision in June 1991, only a few months after the official launch of the project, for a patent application to the US Patent and Trademark Office (Pto) for hundreds of short sequence stretches of *c*-Dna, or complementary Dna, called expressed sequence tags (Ests)20. In 1991-1992, the Nih continued to file patent applications for 6800 Ests. The Dna sequence information was generated by a group involved in a large scale sequencing effort at Nih directed by Craig Venter. The controversy related to DNA sequences erupted in summer 1991, when at a congressional hearing on the Human Genome Project, Venter announced the Nih's decision [Roberts, 1991: 184]. The quarrel on the Nih decision protracted until the early 1994 when Harold Varmus, recently appointed as director of the Nih, decided not to appeal after a first rejection by the Pto.

Although unusual, the virulence of the controversy, that immediately gained an international dimension, can be explained by a variety of reasons.

First of all, the initial move toward the commercialization of genetic information was not made by a commercial organization but by a public institution, an agency of the US genome project. Secondly, the controversy split corporate leaders, industrial associations, legal experts and senior official even inside the Nih. Watson, the leader of the project and director of the genome office at the Nih, strongly opposed the initiative and ultimately resigned. The academic community, in large majority, and scientific societies such as the American Society of Human Genetics and the Human Genome Organization (Hugo), the international non governmental organization dedicated to foster international collaboration in genomic research, expressed fear for the negative impact on research of patents on genome information [Cook-Degan, 1994: 317].

Among the industrial associations in the sector, the Industrial Biotechnology Association (Iba), the membership of which represented mainly pharmaceutical and large biotechnology firms and 80% of US investment in biotechnology, opposed the Nih to adopt a policy of filing patent applications on partial sequences of unknown biological function. Apparently Iba feared that such an upstream patent protection could produce an improper control by the Nih over "more meaningful and costly" downstream research and product development by the industry. Iba also expressed concern that a patent at this stage could in-

[20] An Est is a short portion of a gene that can be used to identify the expressed gene and as a marker to locate the gene in a physical map of the genome.

crease the risk of lawsuits for infringement and hinder research and development of new medical products. The Pharmaceutical Manufacturers Association (Pma) held a rather similar view with the noticeable specificity, however, that the NIH should maintain the existing patent applications until an international agreement were reached, leaving such sequences to the public domain. On the contrary the Association of Biotechnology Companies (Abc), representing the small biotechnology firms, took a favorable stance on the Nih move. Abc supported the filing of partial *c*-Dna sequences prior to publication recognizing, as a possible consequence of publishing partial sequences, the rejection of future patents on full gene sequences with identified biological function on the basis of a lack of novelty or obviousness [Eisenberg, 1992: 907; Adler, 1992: 912-913].

Thirdly, the contention expanded internationally, as many people saw the patent application as an attack to international collaboration putting at risk the whole project. Fear mounted that, in absence of an international agreement on data sharing, a climate of patent gold rush could risk the project to fall apart.

The Ests controversy centered on three major questions:

1. what could be patented;
2. what should be patented;
3. what effects patenting could have on research and industry.

In spite of the roars surrounding the Nih patent application, the way the Iprs process started and developed, and the behavior of the parties in the controversy, fit quite nicely the logic of the US policy-making pattern.

The Nih move was 'preemptive' and 'tentative', directed to defend future options and to test the response of the other parties involved in the issue21. Though patenting was not statutory obliged, it was difficult to avoid it in practice. The legislation of the 80s, as outlined before, delineated a framework for indirect technology policy largely based on the active involvement of the federally funded research performers - universities, public laboratories ad agencies – in actively pursuing technology transfer through patent and license policy. In the face of the Congress and of tax-payers for the Nih it would be politically dangerous if a failure to cover the Ests sequences with a patent application could make it difficult to patent downstream inventions or if, for example, "a

[21] Bernadine Healy, the Nih director, qualified the filings as an "interim policy" and chief of Nih's Office of Technology Transfer, told that the agency devised to sought patent application to protect future options, and to foster public discussion without forcing any outcome or policy decision [Adler, 1992: 908].

Japanese firm grabbed the patent rights for genes, when Nih might have been able to confer a preference for American manufacture through licensing its patent rights" [Cook-Degan, 1994: 311].

In the US, the controversy over the Ests patents never reached the high ranks of the political arena. It remained largely confined to the players, and neither official position was taken nor effort was made by the government to try to forge a common view on the matter. The Congress in fact did not adopted statutory provisions on this issue and left the question of the patenting of Dna elements including genes, Ests, to be resolved by Pto and the courts.

In Europe, on the contrary, the controversy soon escalated to the political center. Especially in France the minister for research and technology Hubert Curien was particularly vocal on the issue and openly pressured the European Patent Office to reject a patent application on more than 2000 *c*-Dna fragments filed by the Nih in June 1992 [Anderson, 1992: 525]. Later in the decade, the European Union in 1998 released a Directive on the legal protection of biotechnology inventions which included specific rules on patentability of full length and partial Dna sequences (such as Ests).

3.3. Celera: a private challenger.

In the mid 90s, the genomic arena took a significant turn, shifting from a sector largely dominated by public actors to a sector in which the more dynamic role moved to the private agents.

The public funded Hgp relied heavily on the commercial sector to pursue its initiative. The sequencing machines and a basic technology such as the polymerase chain reaction (Pcr) were created or developed in a private environment. Beside, the development of a commercial spin-off of genomic-related initiatives was a desired outcome. However, as the advent of new large-scale privately-funded sequencing initiatives occurred at an early stage of the project life, major tensions were inevitable. Ironically, the threat came from Craig Venter, the man who was at the very center of the Nih Ests patent dispute.

Venter left the Nih in 1992, in the middle of the patent contention. After a refusal for funding, he felt frustrated at Nih in its effort to scale up his Est approach to gene discovery. With the financial help of a venture fund he set up a non profit research institute, The Institute for Genomic Research (Tigr), where he was expected to freely continue his research and publish his findings. To recoup its resources the venture fund created a sister company, the Human Genome Sciences (Hgs), to sell the discoveries made by Tigr sequence data. Priority was given to identify Ests from as many genes as possible and to sell access to

Ests data to pharmaceutical partners who can use those data as an aid to identify disease genes. Hgs' first big deal with SmithKline-Beecham, the British pharmaceutical company, triggered a wave of similar liaisons between start-up genomic companies and big pharmaceutical companies [Davies, 2001: 64-66].

However, the real challenger to the public funded Hgp came out in May 1998. Venter and a Perkin-Elmer Corporation, a laboratory equipment company, joined forces in a new privately funded company later called Celera, to sequence the complete human genome. The initiative was made possible by an innovative 'shot-gun' sequencing approach and by innovative sequencing technologies developed by Applied Biosystem Division of Perkin-Elmer (Pe). Press releases following the announcement, maintained that the new company would achieve its objective in three years at a cost of $200 millions, *i.e.* four years sooner and ten times more cheaply than planned by the public initiative. The new initiative, which the *New York Times* (May 12 1998) called "a takeover of the human genome project" and "a venture of unusual audacity", was perceived as a major shot to the public project. In fact the initiative paralleled the core business of the Hgp and commentators were wondering how much longer it would be before public agencies "decided to pull the plug and divert funding elsewhere" [Anonymous, 1998: 195].

Reactions from the public funded project questioned the accuracy and completeness of the new proposed sequencing strategy. Yet, in a replica of the Est sequencing controversy, the debate went on data acùcessibility and intellectual property. Critics objected to Celera's plan of releasing sequence data publicly every three months, not daily as stated in the international Bermuda Accord (1996). The private initiative committed itself to release the complete human genome sequence at the end of the project. As Celera qualified as an information company intended to sell products and services associated with its library of genomic information, placing no restriction on how scientists can use this data, the company established it will seek to develop on its own only 100-300 medically important genes for use by pharmaceutical and biotechnology companies, and to license them on a non-exclusive basis [Venter, 2000].

The public funded project and the Celera scientists were set to engage a competitive course, which hopefully ended in a Pareto improvement for the whole genomic enterprise. The competition was harsh on the issue of sequencing release as Celera was unwilling to follow all the standards set by the public funded scientists. An involvement of the US President and of the UK Prime Minister was to prompt negative side-effects when they issued a joint statement on March 14, 2000, encouraging scientists on both sides "to release raw funda-

mental information about the human Dna and its variants rapidly into the public domain" [Davies, 2001: 205]. The Clinton-Blair statement, interpreted as a move to restrict gene patents, prompted concern causing a plunge of the genomic stock values in the markets. Two days later, the Pto rushed to issue a statement that the US patent policy remained unaffected. The Pto's Commissioner made known that "genes and genomic inventions that were patentable last week continue to be patentable this week, under the same set of rules". Few months later (June 2000), the international Human Genome Project and Celera Genomics Corporation have both completed the initial sequencing of the human genome. Clinton and Blair were ready to congratulate the scientists working in both the public and the private sectors "on this landmark achievement" [White House, 2000].

4. The politics of Hgp: a win-win strategy.

The intellectual property policy of the US government has clearly played a key-role in our Hgp case-study. This policy, which is indeed at the core of the US policy in science and technology, is clearly designed to reward with fair return scientists and companies taking risk in S&T enterprise. The policy and the market-friendly regime which develops is not all the story that the paper has accounted. The US policy is made up of many facets which tell this policy to be very much articulated. The US politics which relies on the Congress and the White House has indeed acted as a catalyst to foster cooperation among the interested parties, and its decentralized policy-making anchored around the intellectual property policy has opened the gate to private agents which at some point in time joined the enterprise and accelerated the final achievement.

The short gene sequencing controversy of the '90s and the institutional dynamic unveils the federal government in its elected bodies assuming the role of an 'arbiter' instead of a 'player'. Federal agencies, indeed, were obvious players in shaping the governance of the genomic industry and in designing an Ipr regime, and behaved like other actors in the sector. In a certain way, the patent reforms of the '80s even compelled the Nih and Doe to act in this way. Yet, the fragmented and decentralized structure of the US bureaucratic bodies kept the political government in a detached regulatory position while pushing other actors from the private and public spheres in the policy arena. This point made a great deal in the dynamic of the policy process and policy outcomes.

As far as the process is concerned, the government never entered in the business trying authoritatively to set the terms of intellectual property protection in genome knowledge. It never tried even to lead the debate and to build a

strong and coherent position on the issue. On the contrary the actors involved, including the Nih, were able and willing to strongly challenge the Iprs *status quo* in a competitive adversarial way, in which independent regulatory agencies -- such as the Pto -- and the judiciary ones played a strong policy role. In fact, because no agency or actor can control the process, for the genome Iprs we can state what Vogel maintains for the US regulatory process in general, that "it tends to progress in fits and starts, with any apparent resolution likely to be challenged at a later stage" [1996: 230].

As this paper has accounted, this policy-making dynamics turned into an incremental open-ended approach and was able to pursue an expansion of intellectual property rights and eventually to favor the new entrants, creating a significant niche for genomics and the genomic industry. If genomics as an industrial sub-field emerged and is on the way to radically transform the biomedical and pharmaceutical sector, in part it is to be credited to the decentralized decision-making process. The model, deeply rooted in the US institutional system, does not allow any single agency or actor to win the game.

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