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Constructing failure in big biology: The socio-technical anatomy of Japan's Protein 3000 Project

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Abstract

This study focuses on the 5-year Protein 3000 Project launched in 2002, the largest biological project in Japan. The project aimed to overcome Japan's alleged failure to contribute fully to the Human Genome Project, by determining 3000 protein structures, 30 percent of the global target. Despite its achievement of this goal, the project was fiercely criticized in various sectors of society and was often branded an awkward failure. This article tries to solve the mystery of why such failure discourse was prevalent. Three explanatory factors are offered: first, because some goals were excluded during project development, there was a dynamic of failed expectations; second, structural genomics, while promoting collaboration with the international community, became an 'anti-boundary object', only the absence of which bound heterogeneous domestic actors; third, there developed an urgent sense of international competition in order to obtain patents on such structural information.

Keywords

anti-boundary object, big science, expectations, Japan, structural biology, structural genomics

Introduction

In 2005, the journal *Nature* published an unusual review of a book that had been released only in Japanese (Ito, 2005). Written by Nobuhito Kishi, a journalist specializing in intellectual property, *Genomu Haiboku: Chizai Rikkoku Nihon ga Abunai* or

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Defeat in the Genome: Japan's National Policy for Intellectual Property in Danger (Kishi, 2004) conveyed a sense of urgency concerning Japan's gloomy economic prospects, which it argued were caused by continuous 'defeats' in an international war for intellectual properties.

Perhaps reminiscent of John Osborne's stage play of that name, Kishi describes his 'look back in anger' about what happened in the Japanese genomic research policy. The opening of his book eloquently reveals his undisguised indignation:

> The traumatic thought weighing on the person's mind straightforwardly narrates the tragedy of Japan's 'defeat in the genome'. His DNA-decoding scheme should have been five years ahead of that of the US … More than twenty years before, at the end of 1970s, he was nursing the original idea of high-speed machine for decoding the genetic information of DNA. (Kishi, 2004: 3–4)

The person referred to here is Akiyoshi Wada, a leading biophysicist whose pioneering steps in proposing an automated sequencer, based upon the Maxam–Gilbert method, are the topic of the first half of Kishi's book (cf. Wada, 2005: 136–138; Wada et al., 1983). Wada launched a project for its development in 1981, which brought together both scientists and leading industries. Later, Charles Delisi, the director of the Department of Energy's Health and Environment Program, was alarmed to find that Japan was 5 years ahead of the United States on the DNA sequencing project (Cook-Deegan, 1994: 215–216, ch. 5).

Kishi eloquently narrates how such Japanese inventions as four-color fluorescent labeling in 1982 and the Capillary Array DNA Sequencer from Hitachi in 1993 (cf. Anonymous, 2001) were ruined by a series of blunders rising out of conflicts between competing ministries, as well as by the shortsightedness of scientists about the possible future of such technologies.[1] Thus, the US Congress, Office of Technology Assessment's (1988) comprehensive report on the prospect of the Human Genome Project (HGP) dispassionately described the weaknesses of Japan's move, and by the end of the HGP, Japan had contributed only 6 percent of the decoding, in contrast with 59 percent for the United States and 31 percent for the United Kingdom.

In the latter part of the book, the tone changes from indignation to hopefulness, and this shift is because of the topic of this article: the Protein 3000 Project, launched by the Japanese government in 2002. Apparently having learned bitter lessons from too-small support and too-late timing, the merged ministry of the Science and Technology Agency (STA) and Ministry of Education (hence Ministry of Education, Culture, Sports, Science and Technology, or MEXT) promoted the project, pouring an unprecedented amount of ¥53.5 billion (US$618 million) into all Japanese teams of structural biologists for a projected analysis of 30 percent – not 6 percent – of the 10,000 protein structures agreed upon by the international community of structural genomics.

In 2007, MEXT's Life Science Committee created a project evaluation plan, concluding that it had successfully attained its numerical targets – 4517 structures analyzed, 3923 registered in the Protein Data Bank, 403 patent applications, and 4195 articles (MEXT, 2007). In addition, one of the studies produced through this project had been cited more than 2000 times (Institute of Physical and Chemical Research (RIKEN), 2008).

'The project has, in quantitative terms, sailed along', commented an article in *Nature* (Cyranoski, 2006). Here, however, lies a mystery: negative assessments broke out in

scientific journals and major newspapers during and after its completion; some scientists questioned the authenticity of the numerical target (Oshima, 2007), while others expressed their frustration with the project's domination of the protein science budget and monopoly over one research institute's grants (Arata, 2008, 2010; Ikura, 2008). An influential newspaper published an article questioning the idea of such a big biology project (Nakamura, 2007), and drug companies were reportedly frustrated about allegedly poor results that did not sufficiently contribute to drug discovery (Anonymous, 2007, 2009).

One of the most damaging criticisms, making an impression on the concerned international community, was the article in *Nature* cited above. There, Kurt Wüthrich, the Nobel Prize winner for developing a method to analyze protein structures through Nuclear Magnetic Resonance (NMR) spectroscopy, was quoted as saying, 'It became a one-man show with 40 NMR machines – there is no knowledge.' Another researcher condemned the project as having analyzed only 'junk proteins' (Cyranoski, 2006). The prevalence of such negative evaluations is even seen online in the automatic tag of *shippai* (failure) that turns up when one looks for *tanpaku* (protein) 3000 in Google.

The mystery that this article tries to solve is the cause of the impressive asymmetry between the apparent success of this project in terms of it attaining its official targets and the subsequent burst of failure discourse.

This article follows the development of this project from the early days of its conception in the 1980s to the period after its completion in 2007. At focus is a particular dynamic of expectations raised by a variety of groups concerning a then-emerging direction of research called structural genomics, an omics approach to the study of protein structures. This article will argue that behind the rhetoric of failure concerning this project lie a number of mutually related factors, namely: (1) inter-institutional dynamism that radically changed the political and research landscape during the period; (2) the highly controversial nature of this new research topic, which continuously produced schism within and without the concerned research communities; and (3) the international context in which this project was embedded.

Theoretical framework

My first task is to sort out how a project can from its beginning be dubbed a failure. Unless the evaluation comes from a clear failure of a project to meet its own goals, the origin of such failure discourse should be sought in the socio-technical context in which it is embedded. In pursuing this, the dynamics of expectations are pivotal (Borup et al., 2006; Brown et al., 2000; Fortun, 2008; Milne, 2012; Van Lente, 1993).

Expectations bring with them emotional connections to hope and hype (Berube, 2006; Brown, 2003); these can even be formulated as Gartner's 'hype cycle' – a simple diagram illustrating a sharp rise in expectation, followed by its inevitable fall, and leading to a more moderate plateau – in currency in the business world (Gartner, 2012; Pollock and Williams, 2010; Van Lente et al., 2013). Although the Gartner hype cycle may be too simplified (Borup et al., 2006; Rip, 2006; Van Lente, 1993), importantly for my purposes it identifies disappointment as an integral part of expectation dynamics. However, the optimism in the model about recovery from the bottom of disillusionment misses the profound consequences that such disillusionment may produce (Borup et al., 2006). Previous

studies have discussed such issues in terms of the difficulty of regaining trust once expectations are betrayed (Brown, 2003; Martin, 2002), the preventive measures taken against such risk by means of legal control (Tutton, 2011), and researchers' efforts to overcome disappointment through more radical research practices (Michael et al., 2007).

In the wider context of the development of projects, multiple expectations in the early stage should be coordinated or 'funneled' (Law, 1986; Van Lente, 1993: 140)[2] into 'incremental trial and error learning' (Collingridge, 1992), with the use of entities such as 'boundary objects' (Star and Griesemer, 1989) and 'ideographs' (McGee, 1980; Van Lente, 1993) to nurture the 'collective expectation' (Konrad, 2006), which is to be materialized by 'selectors' in the arenas of expectations (Bakker et al., 2011). Summarized as such, the sources of the failure discourse around the Protein 3000 Project as part of a disappointment dynamics are likely to lie inconspicuously somewhere in this process because the issue is more about unfulfilled *expectations* than a failed *project*, per se. In this article, I will highlight three factors that I believe to have been instrumental.

One factor concerns a problem that I call 'structural exclusion'. When one expectation gains momentum, others – in the form of both expectation and social groups – may be marginalized or excluded unless their voices are properly subsumed or compromised with those in the mainstream. Collingridge (1992) and Williams (2006) have pointed out both the need and the danger of excluding certain social groups or expectations, if in a rather cursory manner; however, I will fully credit the dynamics of exclusion as being an important issue in relation to the dynamic of disappointment, which previous works have failed to explore thoroughly. My use of the adjective 'structural' signifies that in the following case, this process is intrinsically related to inter-institutional dynamics that enlarge the gulf between what is excluded and what is not – which is the 'prime suspect' in the prevalence of the failure discourse under discussion.

Related to this, the second issue concerns the failure of the boundary object. Unlike the ordinary success stories about it – about the subtle balance needed between allowances for multiple and often contradictory interpretations and the value of sustaining a loose unity among them (Duncker, 2001; Duncker and Disco, 1998; Star and Griesemer, 1989; Stemerding and Hilgartner, 1998), I will examine the condition when such 'magic' is lost or has turned 'black' or malignant. This possibility is immanent in the original concept of the boundary object because its working hinges upon interpretive ambiguity, which potentially causes trouble. In the spectrum from benign (hence successful) boundary objects to disputed issues and uncoordinated actions, I claim there is a certain in-between condition where an entity may work like a boundary object on the surface, although it is actually causing serious schisms. I label this an 'anti-boundary object'.

An anti-boundary object carries a capacity to foster collaboration in one dimension, but may work schismogenetically (Bateson, 1972) in another. Hence, I introduce the prefix 'anti-', partially inspired by entities such as anti-proton or anti-matter in the light of their negative qualities compared with their more common counterparts. In addition, the object can be regarded as manipulative in a sense of hiding schisms occurring in one context to reach consensus in another, which I metaphorically compare to entities such as fallen angels or even the anti-Christ. This notion is instrumental in highlighting the puzzling character of 'structural genomics' in the project, which contributed both to

success and to causing dissatisfaction among those who took it seriously, hence aiding and abetting the prime suspect of structural exclusion noted above.

The third factor was the urgent sense of 'international competition' in which the project was embedded. Any large international project is both collaborative and competitive. Competitive aspects on the international stage, however, have received less attention than issues such as organizational style or methods of collaboration in previous studies on big science (De Solla Price, 1965; Galison, 1992), management of large technical projects (Collingridge, 1992; Disco and Van Der Meulen, 1998), or big biology (Davies et al., 2013; Parker et al., 2010; Vermeulen, 2010). The prehistory of the Protein 3000 Project – including contexts such as the trade war between Japan and the United States in the early days of the HGP – should prompt attention on competition, as the sense of urgency to win the race may have led to further difficulty in coordinating heterogeneous expectations, thus accelerating the exclusion process further. In addition, an intriguing side-effect was the 'flexible implementation' of the big science project to win the international competition, contrary to common arguments about big science projects being implemented in fixed and rigid ways (Collingridge, 1992; Vermeulen, 2010). This unusual 'flexibility' may have raised expectations, even during its implementation, eventually adding another layer of disappointment on top of those already caused by the two other suspected factors.

Background

Structural genomics

In addition to my theoretical framework, two continuos in the pivotal role in the following narratives should be pointed out. One is about the controversial nature of the very research topic – structural genomics – a chiasmic product of translating the idea of genomics to the realm of structural biology. There are two fundamental problems to this new trend, namely, (1) the difficulty of applying an 'omics' approach to protein structures and (2) the question of the seemingly endless diversity of proteins. In contrast with analyzing protein's amino-acid sequences – usually dubbed as proteomics (Chee and Clancey, 2013; Lee, 2015; MacKenzie et al., 2013; Twyman, 2004) – the diversity of protein *structures* has produced the unique world of structural biology – based upon X-ray crystallography, resisting a high-throughput approach (Brenner and Levitt, 2000; Goldstein, 1998; Montelione, 2001).

In recent years, the rise of NMR spectroscopy has been considered a solution for achieving high-throughput analysis of protein structures. NMR was invented in the 1950s for detecting how molecules bind with each other through generated magnetic resonance (Blume, 2003; Lenoir, 1997; Morris and Travis, 2002). In the 1980s, Kurt Wüthrich and Richard Ernst developed the method of applying NMR to macromolecular protein analysis, an accomplishment that secured the former the Nobel Prize in 2002 (Suea et al., 2005).

NMR does not require crystallization of proteins, a feature for which Myers (2008: n. 25) records X-ray crystallographers' jokes that branded its ad hoc nature as 'voodoo science'. Its drawback, however, is its limited analytical capacity; it is restricted to analyzing only the parts or the 'domains' of a single protein (Twyman, 2004; Wüthrich, 1986).

As for the conundrum of seemingly endless variations of protein structures, Chothia (1992) proposed an innovative theory of protein folding that reduces it to elementary 'folds' or structures and their combinations. Although his early estimation of 1000 folds was later increased, his article opened the door to the omics approach to protein structures by limiting analysis to elementary structures, the rest to be done with computer simulation. Thus, 'the determination of as few as 10,000 new protein structures would provide enough information … to model almost all the protein universe' (Bonanno, 1999: R851).

The idea of extending the genomic approach with these two innovations – NMR and Chothia's theory – prompted the rise of 'structural genomics', the omics approach to protein *structures*, which took shape toward the end of the millennium. As Gaasterland (1998) explained, it is 'bioinformatics in the driver's seat' (p. 625), colored with a discourse of a revolutionary future (Gershon, 2000; Hol, 2000).

Institutional background

The second continuo to be noted is the institutional background. RIKEN, the official acronym of the Japanese title for the Institute of Physical and Chemical Research, is the main battlefield. Since its establishment in 1917, on the model of Germany's Kaiser Wilhelm Institute as a national flagship research institute, RIKEN's fortunes waxed and waned until its revival in 1958,[3] as one of the strategic moves of the second institutional protagonist for this article, the Agency of Science and Technology (STA).

STA was established in 1956 as the extra-ministerial board of the Ministry of Internal Affairs for the purpose of the coordination of large-scale science policy, including nuclear energy, space science, and oceanography (Anonymous, 1986; Watanabe Memorial Foundation, 2009: 4). Their new budget scheme, called the Special Coordination Funds for Promoting Science and Technology (*shinkô-chôsei hi*), has been instrumental in launching big science projects (Watanabe Memorial Foundation, 2009: 17–26).

The Ministry of Education, which supervises higher education and research, has been involved in a jurisdiction dispute with STA concerning its big science orientation and RIKEN's position in science policy. In response, STA transformed RIKEN by creating a series of time-bound centers, in contrast with the more traditional headquarters of RIKEN in Wako City, Saitama, with its tenured researchers in about 50 laboratories (hereafter, the 'Wako RIKEN'). This made RIKEN more directly instrumental in executing STA science policy after the 1980s. The inter-institutional politics is also pivotal for understanding the zig-zag itinerary of the earlier project plan that would become the final Protein 3000.

The following sections describe the development of the Protein 3000 Project from its inception by the Wako RIKEN biologists in the 1980s to its actual enactment and the aftermath in the 2000s. I identify three distinctive phases in the development of the project. In each phase, the composition of the main characters and their expectations changed almost completely, the changes caused by various levels of inter-institutional conflicts, growing controversy about the meaning of the emerging structural genomics, and the international collaboration and competition that gained momentum as time passed. All of these entangled elements resulted in not only discontinuity from the previous phase but

also voices of disappointment, misunderstanding, and even indignation at various levels. This eventually led to the prevalence of *shippai* (failure) discourse, despite the fact that the project was seemingly successfully launched and had even attained its initial goal – important after the preceding 'defeat in the genome'.

Research method

The research on this project was divided into two phases. The preliminary part, from 2007 to 2009, was part of an ethnographic study of an antibiotic laboratory in RIKEN (Fukushima, 2013) on the development of natural products chemistry and chemical biology. During this period, I conducted pilot interviews with the participants of the earlier Protein 3000 in the lab. This enabled me to identify the outline of the issues as well as key persons to be accessed in the following phase.

The main research took place from 2010 to 2013; it was based upon semi-structured interviews with 17 central actors, concerning both their roles in the project and their general views about such project at large. These were scientists and officers, selected from the aforementioned pilot studies, who played leading roles at various levels, from the project's planning to its implementation in and out of RIKEN. The interviews were supplemented with archival reviews of journal articles, policy documents, proceedings of the project, newspapers, and so forth. Attention was paid to RIKEN's pivotal role in the project, as the majority of the later criticism more or less concerned with the institute. All interviews were recorded and then transcribed. Although I made a great effort to collect key policy documents, quite a few have been lost owing to the present ministry's repeated restructuring and moving.

Phase 1: The birth of the idea of 'the NMR Park'

In the 1980s, the X-ray facilities in KEK (High Energy Accelerator Research Organizations; cf. Traweek, 1988), supervised by the Ministry of Education, and RIKEN's construction of SPring 8 (Super Photon ring-8 GeV), the world's largest radiation facility (Interview 6), marked the consolidation of research infrastructure for protein science. By way of contrast, two laboratories were to be noted for the introduction of NMR machines specifically for protein analysis: one at the University of Tokyo first introduced the cutting-edge superconductor NMR by Bruker Ltd. in 1976, while another at the Osaka University purchased NMR equipment in 1980 (Tasumi, 2006). The former laboratory produced the later leaders of the Protein 3000 Project, while the latter exerted extensive influence on the whole community of structural biologists.

At the Wako RIKEN, Takehiko Shibata, a specialist in the homologous recombination of DNA, took office in 1985 and launched the Bio-Design Project to promote the life sciences and to raise their status there; this involved all 10 of RIKEN's genomics and structural biology laboratories. In 1993, Shibata invited Shigeyuki Yokoyama – later one of the general leaders of the project – to RIKEN to establish a structural biology laboratory (Interview 4). Yokoyama was a graduate of the above-mentioned lab in Tokyo, specializing in DNA–protein interaction using NMR, a rare specialty because of NMR's limited capacity at the time. In the early 1980s, Shibata had already been impressed with

Yokoyama's claim for the merits of NMR in analyzing the ligand–protein interaction within solutions, which could solve Shibata's own research problem (Interview 4). Another proposal from Yokoyama also prompted Shibata to introduce NMRs:

> We also thought that we could gain support if we had an international NMR center open for use throughout the country [as proposed by Yokoyama], because it is hard to have and maintain cutting-edge NMR machines in a lab or even in an institute. (Interview 4)

Thus, in 1994, Yokoyama launched the idea of a comprehensive analysis of the elementary structure of proteins using '100 NMRs' in the Bio-Design Project. The official historiography of RIKEN comically describes the shock of a senior chief researcher, who suspected that Yokoyama had lost his marbles (RIKEN, 2005); such a concentration of NMRs in one place was unprecedented both within Japan and elsewhere. Yokoyama later explained at least two reasons behind his exorbitant proposal: first, Chothia's (1992) article on elementary structures of proteins convinced him of the feasibility of a comprehensive analysis of protein structures (Oshima et al., 2002b: 867). Second, there was a twist in the numbers of NMRs that he wanted:

> I said eight NMRs, not 100, but they [the physicists in the Wako RIKEN] asked if I was sane. They said that even if we had eight NMR machines of 600 MHz, the total size is 2.4 GHz or so, which, they said, would not lead to new science. (Interview 19)

The idea of 100 NMRs was instigated by nuclear physicists in the Wako RIKEN, who were accustomed to big facility proposals in terms of accelerators: Shibata and others testify that ¥10 billion (US$100 million) was the basic unit of a big proposal there (Interviews 4, 11). Yokoyama emphasizes that the idea of simultaneously purchasing several machines of similar size was then novel:

> Even Wüthrich later asked me what I was going to do with the machines when world NMR researchers rarely bought even two of the same size. But in reality, after we had the NMR facility here, similar things happened in the rest of the world. … Our plan was ridiculed as 'the project of buying NMRs', but in fact there were rapidly expanding needs for protein analysis, so we had to respond to them. (Interview 19)

The 100 NMRs proposal obtained approval in snowball fashion, swiftly ascending the ladder of RIKEN's and STA's bureaucratic machineries (RIKEN, 2005). STA needed a big-budget project to consume a surplus budget after the completion of the nuclear-powered ship Mutsu (Interviews 4, 11).[4] An add-on booster for the NMR project was the idea of sequencing the whole protein structure of *Thermus thermophilus* for medical purposes. *Thermus* is a gram-negative Eubacterium that resists high temperatures – discovered in a hot spring in Japan – that produces easy-to-crystallize proteins. Seiki Kuramitsu, a biochemist from the Osaka University, had long nursed the idea and Yokoyama, soon after becoming acquainted with Kuramitsu in 1995, adopted it; Kuramitsu was later one of the main leaders of the Protein 3000 Project, along with Yokoyama and others (RIKEN, 2005; Interview 18).

Rising expectations for 'the Park plan'

In the process of this administrative legitimation, two contradictory tendencies gradually emerged: the growing expectation for the *communal* use of NMRs and the plan to go beyond such a scope. The NMR plan, later named 'the NMR Park', was intended to be a common facility open for international use (Interview 4; cf. Vermeulen, 2010). The spread of the news of this plan elicited various reactions ranging from wholehearted approval to restrained skepticism. Shibata summarizes the atmosphere of this stage of the plan:

> Thus, there was widely shared support for the idea of such facility, shown for example in the reports in the *Nature* journal around 1997 [sic]. What was supported was the facility's being open to international use. And they also supported it because this facility is also contributing to enhance Japan's presence in this field. (Interview 4; cf. Swinbanks, 1996)

A number of people commented on the international support:

> In fact, researchers both in Europe and the US strongly welcomed the idea, because they could make use of this precedent: 'Japan spends such money, so should we.' (Interview 3)

> So at that time, researchers in India, for instance, were enthusiastic about the plan, saying 'If there is such a plan, we are keen to participate in it. Let us use them.' Now the Indians are rich enough, no need for it any more, though [laughter]. (Interview 7)

Domestic reaction was more varied. Certain expectations seemed to have risen among younger generations of researchers:

> [Admitting the later criticism on the project] At the moment, among the younger generation, there was surely approval of the plan. … I don't believe that those who were not established in their academic careers … had only bad impressions of [the Park plan for] developing an environment where you may make use of a machine of 900 MHz with only the slightest effort. (Interview 8)

More senior NMR specialists had mixed reactions:

> When it [the Park plan] was announced … their [the attendants of the NMR seminar] reactions were 'Wow!' or 'That's great!' … Well, the meaning of 'that's great' was probably they didn't believe that it would actually take place. (Interview 10)

Despite a few skeptical voices, these various witnesses point to the general rise of expectations among NMR researchers. However, things turned in an unexpected direction when a couple of new factors came onto the scene.

In sum, this phase was important not only for the project but also for establishing the research infrastructure urgently needed for structural biology, which, at that time, lagged far behind that of other countries. STA was also redirecting its policy toward newly emerging biological fields. Its attention to the pivotal role of RIKEN in actualizing a new

direction of research coincided with a bottom-up movement of biologists promoting emerging biological fields and a brand new tool, NMR. Thus, a happy coincidence occurred in the meeting of goals of some cutting-edge biologists and big-science-oriented policy makers, which created expectations of communal NMRs. But this accidental amity would soon disintegrate, and hopes would turn sour.

Phase 2: Transformation of the NMR Park

In Phase 2, the subject of the project was radically enlarged both in policy and in institutional context, where the process of funneling the multiple expectations was affected by a drastic change in the institutional configuration. The nexus of the project would eventually move from the Wako RIKEN to the newly emerging Genomics Science Center (GSC), RIKEN, with a new main character on the stage: Akiyoshi Wada, introduced above in connection with *Defeat in the Genome*. In this process, the negative effects of excluding various expectations gradually came to the fore. This development was also pursued with the sense of urgency vis-à-vis a rapid international development concerning patents on protein structures.

The rise of the GSC, RIKEN

The initial trigger for this radical change from the earlier plan was an inspection by the Ministry of Finance, which demanded two things. First, it wanted RIKEN and STA to wrap up their mushrooming individual life science projects. This was during the time when the HGP was challenged by Craig Venter's Celera Genomics in 1998 (Venter, 2007). There were a number of HGP-related projects in Japan, such as four national teams participating in the HGP, including one from RIKEN (Shimizu, 2000), the mouse cDNA project in RIKEN's Tsukuba Center (RIKEN, 2005: 329–351), and the NMR Park plan. In response to this demand, Akito Arima, ex-Minister of Education and later the President of RIKEN, commissioned for the task his old friend, Akiyoshi Wada, who had retreated to a small research institute after retiring from the University of Tokyo (Interview 20). Wada responded by restructuring the research as the 'New Life Science Plan', under the banner of 'omics space'. This was designed around a schematic diagram situating genomic and post-genomic life science in terms of five layers: genome, transcriptome, proteome, metabolome, and phenome (Wada, 2008: 67–68). A former officer of STA who later joined RIKEN's managing board testifies to his personal impression of the impact of Wada's perspective:

> The greatness of Prof. Wada is to situate protein research within the whole structure of various omics. So far as I know, there was no one else who did it at that time. I truly believe that Prof. Wada is a great person. … At first he made clear the whole hierarchical structure of omics, and then underscored the importance of attacking on all these levels with quantitative data analysis, which, he declared to the world, was the strategy of life science to come. This is extraordinary. And we now know after genomes, it's proteins. Proteome. (Interview 14)

Eventually, Wada's comprehensive omics plan led to the establishment of the GSC in the Yokoyama RIKEN in 1998 (RIKEN, 2005). Seen from the Wako RIKEN, however, it looked as if their own plan was alienated:

> There were cases in which our proposal did not pass in RIKEN's managing board. … We developed a plan for a collaboration team with GSC … but eventually it was not accepted. … In short, it seems to us that Prof. Wada did not want to be inconvenienced by the ancient regime of RIKEN, which he may have thought could become annoying. (Interview 4)

Behind this growing rift between them, the former STA officer quoted above corroborated the long-term intention of STA's intervention into the direction of the GSC as playing a role in policy objectives (Interview 14). Later, Wada himself seems to have acknowledged the character of his center as 'running alone' vis-à-vis the old Wako RIKEN:

> There was an interesting structure, in terms of RIKEN's managing board. They came from STA, and when we established GSC, in STA I had my old friend …, who thoroughly supported GSC's running alone. And [citing a few names] STA sent all their aces to GSC, so that's maybe the reason why GSC looked like an independent fortress [*shiro*] against the Wako RIKEN. (Interview 20)[5]

Structural genomics and its discontents

Such inter-institutional conflict was accompanied by turmoil about the rising currency of the idea of structural genomics, partly related to a second thing that the Ministry of Finance wanted for RIKEN: to prove the validity of such a large facility in an international context (Interview 11). Thus, Yokoyama and others traveled to the United States and tried to impress their counterparts:

> We went to a meeting to discuss NMR facilities in the US, and our story about the same 100 machines on line was printed and presented as if we were about to launch this, and I heard afterwards that the US side realized that they would face a serious problem if they were caught off guard. … I heard that there was an 'NMR Park shock' in the US. … At that time our copy of the plan we distributed there circulated throughout the US where it became worn out. (Interview 19)

As if corroborating this alleged 'shock', the official chronology of the International Structural Genomics Organization (ISGO, 2013) traces its history from Yokoyama's 1995 proposal at RIKEN first, followed by a series of international reactions, such as the US' 1997 New Jersey Initiative and the Workshop on Structural Genomics in the Argonne National Laboratory. The latter institutionalized the name of the international project as 'structural genomics' (Terwilliger, 2000).[6] These events were followed by the *Nature Structural Biology* special issue, which was devoted to structural genomics in the United States (Terwilliger, 2000), Europe (Heinemann, 2000), and Japan (Yokoyama et al., 2000a, 2000b). Meanwhile, in a subsequent conference in Virginia, the ISGO was officially launched and was instrumental in setting a target of 10,000 protein structures to be analyzed in international collaboration (Smaglik, 2000).

Here, however, the controversial character of structural genomics – eventually as an anti-boundary object – gradually emerged in the shape of suspicion of its basic assumptions by structural biologists. First, the senior NMR experts who Wada consulted as he wrapped up his comprehensive plan – Yoji Arata, Kurt Wüthrich, and other senior members of NMR research – expressed their skepticism about structural genomics.

Among others, Arata, another pioneer of NMR research on protein structure, who launched the NMR Society of Japan in 2002, kept his distance, compared with Wüthrich's more active involvement in the Park plan *per se*, which can be seen in the former's general disbelief in the validity of genomic approach at large: in fact, Arata boasted of his more time-consuming method of determining the large structure of immunoglobulin of 150,000 molecular size – which even Wüthrich's method could not attain – by labeling strands with ^{13}C, which he believed is more reliable than other methods discussed above (Interview 7)

Although not as blatantly, other leading structural biologists in Japan also voiced their skepticism about structural genomics, highlighting fundamental differences between their approach and that of Yokoyama (Yanagita et al., 1999). In further discussions in 2002, a leading bio-informatician openly questioned the basic assumption of structural genomics: namely, the idea that the *functions* of proteins could be understood by comprehensively analyzing their *structures* (Oshima et al., 2002b). Even Yokoyama did not appear to be fully convinced by the international trend: he expressed discomfort about the Virginia conference that was dominated by bio-informaticians such as John Moult and Chris Sander from the United States, who seemed to him to disregard the need to improve high-throughput machinery for structural analysis (Oshima et al., 2002b).

The urgent issue of patents

Despite such smoldering suspicions, the perception of the international situation caused the Japanese participants at ISGO to realize the impending threat of the US move (cf. Meyers et al., 2000). As Yokoyama reflects,

> Then the story was that the PSI [Protein Structure Initiative] in the US was about to launch. At that time, it was said that patents could be acquired for protein structures. And it was the time when the US was securing patents for cDNA, so we were alarmed that it will be lethal if the US monopolized the patents of protein structures. … It was a bit hypocritical of the US to insist on making the information [of protein structure] open to the public immediately because it is only the US that has the industrial capacity to make it profitable. We strongly countered that Japan did not have such capacity while we are doing this project through the support of the state, so we opposed the idea of immediate opening of the data. (Interview 19)

The momentum, especially because the international competition, prevailed over the suspicions among structural biologists, and there was soon a push toward the final Protein 3000.

In sum, in this phase, the plan for the NMR Park, a vague product of researchers' dreams, rapidly transformed into something utterly different. Inter-institutional struggle, for instance, was pivotal in transforming the center of gravity for the project, when STA showed its commitment to promote the plan as national policy in the midst of international competition. This eventually marginalized the promoters of the earlier plan for the NMR Park. The changes were accompanied by a growing schism among leading biologists regarding the very significance of structural genomics, even as, ironically, the new genre of research gained momentum on the international stage, accompanied by growing

competition between Japan and the United States. Hence, the emerging 'structural genomics' started to show its peculiar character of both creating schism among biologists domestically and providing a space for collaboration internationally, beginning to become a puzzling anti-boundary object.

Phase 3: Protein 3000 as national flagship project

In Phase 3, until the actual launch of the project in 2002, further institutional changes took place that again radically changed the landscape of the project. The monopoly of the RIKEN-STA alliance was disrupted to open the project to a broad array of Japanese researchers. In this process, a fatal blow was struck against the idea of the NMR Park, while the plan to analyze 3000 protein structures was finally staged as the central agenda. The changes had a decisive impact on the nagging criticism about the project that had persisted even after its launch.

Changing meaning of the project

Two important administrative events should be noted. The first was the Millennium Project, launched by the government in 1999, to promote important national scientific projects for the new millennium. This big-budget scheme finally afforded the comprehensive plan a final go-ahead as a package (Interview 14). The second event was a large-scale reorganization of the government offices in 2001, in which there was a merger between the competing STA and the Ministry of Education to become the Ministry of Education, Culture, Sports, Science and Technology (MEXT) (Oda, 1998). The project became shared across research communities in Japan, rather than being a RIKEN-STA monopoly: university researchers as well as traditional crystallographers and even bio-informaticians became eligible for grants (Interviews 16, 19).

Why was the target 3000 protein structures? Yokoyama's collaborator details its background:

> At that time, there was a sort of policy catch phrase, 'the scientific and technological nation' [*kagaku gijutsu rikkoku*], and Japan wanted to bear 30% of the world's science and technology. A bit high-handed if looked at now, but at that time, in response to 'the defeat in the genome', the catch phrase circulated in the world of planning the budget. … And at that time the domains of proteins were said to be 10,000, even if it is more now. Thus, 30% would mean 3000. (Interview 16)

Although this target number itself would later invite criticism, even from its promoters, as more political than scientific (cf. Arata, 2008; Oshima, 2007), Yokoyama claims that he then thought it was feasible. *Thermus thermophilus* has only 2000 genes, and it was believed that it could contribute half of the 3000 protein target (Interview 19).

A thorny issue was how to allocate 3000 targets among the various participants. Besides RIKEN, there would eventually be eight different hubs, divided according to topics ranging from development to metabolism, involving both universities and research institutes (Oshima, 2007).[7] After tough negotiation between Wada's GSC and crystallographers in

universities, only 500 proteins in total were finally given to these hubs, as they claimed it was the limit for them as a whole, and the rest stayed at GSC (Interviews 16, 19).

The death of the Park plan

This enormity of the task imposed upon GSC – analyzing 2500 protein structures in 5 years – further brought about what was probably the most controversial decision concerning the nature of the project: GSC decided to restrict the use of 40 NMRs, which had been rather unexpectedly provided to GSC, for use in the project, making them off-limits to outsiders. This decision symbolized a complete break from the original conception of the NMR Park with open access, and this decision aroused a storm of indignation from the concerned NMR community. Here are comments from the original Bio-Design side on the decision:

> It was far from what I thought ideal … The reason is, it did not become a center that everybody wanted … I mean, open use. And if it had been open, there would have been a lot of visitors from all over the world. And that would have facilitated the determination of new structures faster than the comprehensive research on elementary structures … Well, I tried to persuade them to open one or two machines, but was not accepted. (Interview 4)

A noted structural biologist also describes the NMR community's reaction:

> Nobody could use them. And that was the point most severely criticized by NMR researchers about Protein 3000. Even Dr. Shibata could not use them [because he wouldn't have wanted to use them ahead of other researchers]. (Interview 10)

Wada, then a director of GSC, also witnessed the reactions from leading figures of the NMR community:

> Prof. Arata [senior NMR specialist] demanded of me to make the NMRs open to university researchers. Behind him there were a lot of NMR researchers, so I suppose there should have been pressures from them too. … What Wüthrich repeated to me was 'You talk about NMR Park. A park is the place where anyone can enter. But what about it now? It is not a park, it's a private house.' (Interview 20)

From the implementers' side, the story seems more complex. For one thing, the legal basis for the project became what is called 'the intra-ministerial budget' [*naikyoku-yosan*] within the merged MEXT. It stipulated that the contract was 'commissioned' by the government to the contractors, with no openness allowed (Interview 19). The former officer of STA clarifies the policy makers' viewpoint:

> If I had heard the plan of the 100 NMRs [Park plan] and Protein 3000, I would not have bought the 100 machines idea. … [discussing the brain research center in RIKEN as an example] when we heard the discussion of the future of brain research, it was our role to make clear the concrete plan that could be attained in five years. The planning based upon the ideas and intentions summarized by researchers are totally different from formulating the research project, having significance as national policy, from all these plans. (Interview 14)

Yokoyama also points out it was a matter of survival for RIKEN, which was responsible for this national flag project and which could not afford to fail (Interview 19). Wada stresses the difficulty of managing the project had it been open:

> It would have been a big problem if we had opened 40 NMRs for international use. … As I have repeated, the idea of GSC was a factory of mass production of biological data. … So if people came and said 'This data is mine, this data is mine', then it would have been uncontrollable. (Interview 20)

In sum, this phase solidified the irreparable schism between those within the scope of the project and those who were eventually excluded. The once-in-a-century reorganization of the ministerial structure fundamentally changed the nature of the project from that of STA-RIKEN to the all-Japan project. The related legal stipulation almost completed the process whereby the promoters of the earlier plan were excluded, and voices of negative (even emotional) reactions ensued from the marginalized. At the same time, the general haste to launch the project, caused also by accelerating international competition, which was accompanied by the almost impossible task of analyzing 2500 proteins, made the project vulnerable to various levels of criticism, which betrayed a poor understanding of what the project was all about.

The launch of the project and its aftermath

Thus, we have traveled a long way: the final outlook of the project had left almost no trace of the earlier image of the NMR Park as open for international use. The headquarters moved from the Wako RIKEN to GSC in Yokohama. The early sympathizers for the Park plan were marginalized, whereas newcomers from various universities and disciplines were installed under the supervision of the new ministry, MEXT. Thus, voices of discontent rising from the series of exclusions had already accumulated when the project was launched in 2002.

GSC as super center

The enormity of the task of analyzing 2500 protein structures made GSC a sort of super center, a concept that Hilgartner (2013) writes was avoided in the case of early HGP in the United States. For attaining its goal, GSC had to maximize both the crystallographic capacity of SPring 8 and the 40 newly purchased NMRs. GSC rapidly hired approximately 300 new staff, post-docs, and technicians in 19 research units. For speedy analysis, factory-like pipelines were needed, starting from finding genetic sequences from various sources, followed by systematic expression of proteins, which were then sorted according to crystallizability, either for SPring 8 or for NMRs (Interviews 3, 9, 12, 15).

Unlike the fully computerized sequencing in the case of genomics (Stevens, 2013; Venter et al., 1996), automation was only partially available in certain parts of crystallographic procedures at SPring 8 (Interviews 5, 15, 18). In contrast, NMR was more labor-intensive (Triendl, 2001) and new members, stationed to individual research units, were obliged to process compartmentalized assignments (Interviews 3, 9). Through this

process, the meaning of structural analysis also changed because the researchers could not find a sort of periodic pattern of such elementary structures. They changed to simply annotating each of the collected structures (Interviews 9, 17, 18).

New expectations for drug discovery?

There were changes to the project even after its launch, in response to new expectations that arose *during* its implementation (contra Collingridge, 1992; Vermeulen, 2010). This phenomenon was partially caused by the smooth attainment of the target number in the first half of the project period, after which officials set new expectations around drug discovery. As Yokoyama witnesses,

> We realized at the time that after the intermediate review, such an explanation as 'the success of this project leads to drugs' was in currency [among policy makers]. … In the case of the HGP, everybody knows that observing a base sequence does not make you think of drugs, but in the case of proteins, unfortunately, people may think that the determination of the active site of protein may lead to drug design, and if so, we had to take it seriously. (Interview 19)

He also points out the international factor:

> The meaning of the project changed because of the change in the American situation. The US was already in the production phase before we started on Protein 3000 … and this is why we were in a hurry. But then what the US would do after, well, it would be about disease. … So we argued that things related to disease should be done. (Interview 19)

This change, however, caused difficulties because mammalian proteins, the targets of drug discovery, are usually harder to crystallize than those of *Thermus thermophilus* that they had previously used (Interview 12).

In addition, the supervising committee became stricter about monitoring numerical targets, so that the final year was marked by problems in determining analyzable proteins, because generally more complicated ones remained (Interviews 10, 12, 15).[8] On this point, Kuramitsu, co-director with Yokomaya above, rather cynically reports the reaction of his friends abroad on the unusual 'flexibility' of the execution of the big project like this:

> Well, it was something foreigners often said to us. Abroad, once a 5-year project is launched, they first make the goal, and when they decide to do it, the budget and other things will be given as decided. In Japan it is interesting to find that you change your direction and the budget can be decreased. Well anyway, it's awful. (Interview 18)

The aftermath

In 2007, MEXT's Life Science Committee concluded that the project had successfully attained its numerical targets. In terms of equipment, their report enumerates numbers such as 99 NMRs and 226 X-ray detractors, the development of beamlines at RIKEN's

SPring 8 and at KEK's Photon Factory, technological innovation with regard to expressing proteins, a micro-crystallization manipulator, automatic X-ray detraction, and so on (MEXT, 2007).

However, there were critical voices throughout. In 2002, an economic journal published an article questioning various aspects of the project, such as MEXT's managing capacity, the scientific justification of 3000 targets, and the quality of the collected data (Masuda, 2002). After completion, the chair of the project's Promotion Committee revealed in an interview his frank view on the merits and demerits of the project, including the political nature of the target's being set at 3000. The article also compiled existing criticisms, including the lack of patents, data registration delays, human resources, and excessive costs (Oshima, 2007). Referring to this interview, a well-known biologist, acting as the head of the Life Science Museum, launched a critique of the project in an influential daily newspaper, comparing it with the Cancer Genome Atlas Project in the United States and condemning it as being hastily conducted without scrutinizing its scientific meaning (Nakamura, 2007; cf. Isaji, 2009). Despite Wada's (2007) swift rebuttal, her critique ignited heated controversy on the issue, primarily online.

The following year, a protein research journal published a special issue on the project (Tsukihara and Nakamura, 2008), in which a number of articles criticized issues such as the uneven distribution of grants and the project's economic accountability (Ikura, 2008; Hakozaki, 2008). Yoji Arata – then becoming one of the most vocal critics of the project – was unrelenting: he denounced the project for failing to innovate NMR-based protein analysis and for having no impact on either science or drug discovery. He attributed this failure to the general malaise of Japanese science policy, which he characterized as opaque and lacking in legitimacy (Arata, 2008, 2010; Interview 7). This accusation echoes Wüthrich's in the *Nature* article mentioned earlier (Cyranoski, 2006). Both promoters and critics acknowledged that Wüthrich's negative perception of the project as having created 'no knowledge', and an additional remark about 'junk proteins' by another structural biologist, seriously damaged the project's international reputation (Interviews 4, 8, 19), despite rebuttals by the international team (Yokoyama et al., 2007).

The widespread effect of such controversy is evident in a science policy budget commentary in another influential newspaper in 2009, which introduced the project as an example of failure: '[This project] was meant to develop new drugs by analyzing the structure of disease-related proteins, but it fell short of answering such expectations' (Anonymous, 2009).

Discussion

The Protein 3000 Project was originally intended to overcome what was called 'the defeat in the genome'. From the perspective of Kishi's book by that name, the Project should have passed the trial with several factors in its favor: the clear vision on protein research based upon the idea of 'omics space', STA's determined support for Wada's GSC to take initiative in the international community of structural genomics, and the unprecedented scale of a budget that enabled a contribution of more than 30 percent of the international effort. Understandably, official reports were positive.

Expectations marginalized and excluded

Against such a positive evaluation, the possible sources of the harsh criticisms have to be explained. A first source was the process of funneling and excluding earlier expectations, which was influenced by a series of discontinuous development in inter-institutional dynamics. The early NMR Park plan was gradually eroded, replaced by a national flagship project in the Protein 3000 project.[9] In each phase of its transformation, the center of gravity also moved and was accompanied by the marginalization of those who were committed to the earlier ideal – namely, those from the Wako RIKEN who favored an open Park, the senior experts of NMR seeking for a new horizon for NMR's expanded capacity, and, finally, quite a few of the NMR community who were excluded from access to the 40 NMRs at GSC. A consideration of these changes is essential for understanding such criticism about the 'opaqueness' of the planning process (Arata, 2008, 2010), as it seems that even the promoters were not able to foresee such changes.

Structural genomics as an anti-boundary object

However, the foregoing explanation leaves questions unanswered. For instance, why did discourse like 'no knowledge' or even 'junk proteins' prevail in public journals like *Nature* (Cyranoski, 2006)? Why was it claimed that the project was of no use to drug discovery (Anonymous, 2007, 2009)? The second source of the failure discourse, then, seems to have been structural genomics as an anti-boundary object.

One of the impressive idiosyncrasies of this project has been the sharp distinction between its international positioning as a project of 'structural genomics', and its actual implementation by traditional 'structural biologists'. The gulf between them can be seen in the comments of a leading structural biologist in the project, who emphasized that the informational assumptions of structural genomics do not enable an analysis of the subtle relations between the structures and functions of proteins. He also added that in the United States, structural genomics and structural biology are different species, segregated in terms of their funding (Interview 10; cf. Oshima et al., 2002a). Corroborating such a gulf were the harsh exchanges between researchers in the United States on the alleged success of the Protein Structure Initiative (Gerstein et al., 2003; Service, 2002). Pellegrini (2005) contended that the larger community of structural biologists was dissatisfied with the outcome of the initiative, which dealt only with simple structures in contrast to the heroic efforts of crystallographers in analyzing large macromolecular complexes (see Abbott, 2005 on its success).

Not resolving this difference fueled the failure discourse. The expectation and ambition of quite a few NMR specialists were to tackle proteins of a large molecular size by expanding the limits of NMR. In contrast, the Protein 3000 Project used NMR to analyze only small 'elementary structures', based upon Chothia's (1992) theory and bio-informational assumptions. In fact, Kuramitsu confirmed that only he and Yokoyama were somewhat faithful to the creed of structural genomics (Interview 18), Wada being added as the godfather of 'omics space' (Interview 20). A GSC unit leader confirmed that it was only the bio-informaticians *abroad* who generated various findings using the database (Interview 12), whereas a leading bio-informatician in Japan acknowledged the limited role of bioinformatics in the project (Interview 17).

The notion of an 'anti-boundary object' is useful for describing this odd situation. In the project, despite its somewhat misleading appeal to the international community, the concept of structural genomics worked only in its absence to combine domestic actors: the majority of the participants from universities did not seem to take this concept too seriously as their assignments were eventually to determine the structures of a few proteins, compared with 2500 for GSC. Borrowing Schrader's (2010) argument of the 'phantomatic' ontologies of the controversial fish killer, it may be tempting to call structural genomics a 'phantomatic discipline' whose nature as a discipline is seriously disputed. But structural genomics worked concretely rather than phantomatically, with contradictory effects; hence, the term 'anti-boundary object' is more apt to describe the complex situation wherein this genre of research is situated, which eventually led to criticisms such as 'no knowledge' and 'junk proteins'.

Usually, a successful translation between actors by means of a boundary object is observed in a single dimension, so to speak. In the case above, however, the translation matters in two different dimensions: one is within the project itself, and the other is in the international context. What matters here are the divided functions of the same object – namely, failure in one dimension and success in the other. The success demonstrated on the international level is not only misleading (hence, 'anti-' in a manipulative and quasi-theological sense) but domestically it may actively give rise to disputes so that it is better for it to be avoided (hence, 'anti-' in the sense of being contrary to creating harmony). Thus, alternative expressions such as 'failed' or 'misaligned' boundary object will not illustrate fully this complex situation as they are confined to a one-dimensional perspective.

The project in the international competition

We can see some of the problems of the Protein 3000 Project if we compare it with the subsequent Targeted Protein Project (MEXT 2011), which seemingly sailed along without much ado. There are a couple of reasons for this: one is that the subject of this subsequent project returned to a more classical concern in structural biology – membrane proteins and those of large molecular size, which are important as targets for new drugs – without any further trace of structural genomics therein.

The way that the projects were planned and implemented was manifestly different, as illustrated by a comment by Yokoyama's collaborator on this issue:

> [In the case of Protein 3000] there was not much time to do it meticulously. For Targeted Proteins, I had been a member of its preparation committee for three years and we carefully compiled various reports, but in the case of Protein 3000, no time for that. Only one or two conferences … It was far rougher than now, indeed. (Interview 16)

The 'roughness' of the way the Protein 3000 Project was planned is partially attributable to the urgent atmosphere of the time, when many international issues – such as the trade war, the HGP, Celera Genomics, fear of the monopoly of patents, and so forth – were entangled. We have already observed that a sense of urgency dominated its promoters vis-à-vis its international rivals in the various steps of its development. Even at the end, the rise of expectations of new drug discoveries was prompted by a rival's perceived move in that the direction.

Persisting repercussions of the project

The immediate above contrast in styles of management reminds us of Collingridge's (1992) claim concerning the central importance of incrementalism and of trial and error learning in big projects. However, I doubt that the problem would have been solved even if Collingridge's proposal had been practiced during the Protein 3000 Project, and one final episode may illustrate my point. A variety of NMR researchers emphasized the recent progress of the research on so-called intrinsically disordered proteins – proteins without proper structure (Chouard, 2011) – which may provide renewed opportunity for NMR to prove its potentiality. They are chagrinned, however, that new investment into NMR is now out of the question because of the earlier huge omics-inspired investment (Interviews 4, 7, 8, 10).

Thus, while Wada of GSC praises the value of these 'data' for coming generations (Interview 20), an opponent describes the 40 NMRs at GSC as 'a huge wreckage of extravagance in the shape of a ghost town' (Arata, 2010: 161). Similar contrasts can be seen in the life sciences at large, in the differences between traditional approaches and those based on informational orientations (among others; Fujimura, 1999; García-Sancho, 2012; Kay, 2000; Lewis and Bartlett, 2013; MacKenzie, 2003); the tension between these orientations seems to prevent Collingridge's solution from being fully effective in erasing the voices of failure, the difference being apparently almost unbridgeable, at least in this case.

Conclusion

In the context of domestic science policy in Japan and global competition for post-genomic science, the Protein 3000 Project provides rich material for reconsidering the various assumptions of diverse research areas. First, this case study demonstrates that developing a particular policy idea by funneling multiple expectations into a concrete plan has a darker side of excluding certain elements; such an approach may lead to continuous criticism, resulting in eventual devaluation of the very project itself contra its attaining the goal. This is especially the case if the funneling takes place haphazardly, driven by outside events – such as, in this case, changing institutional structures. Thus, the role of the neglected side of failed expectation, disappointment, and even persisting frustration deserves further research without being confined to official reports but involving the wider realm of society at large.

Second, boundary objects – which are usually expected to bind heterogeneous elements benignly and loosely in pursuit of a goal – can also have a darker side. The anti-boundary object functions with Janus-like faces to bind together at one level, but to betray at another by creating schisms when it is fully activated.

Finally, the fierce sense of international competition embedded in this project urges reconsideration about the basic assumptions of recent arguments about big science/big biology, which have been tilted toward underscoring collaboration when competition may have larger effects.

This analysis of the sources of a discourse of failure is a good lesson in learning what not to do in order to avoid the long-lasting aftereffects of the dark side of unfulfilled

expectations. Otherwise, any project – the product of many dreams – may turn for some into a haunting nightmare.

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Notes

1. One of the pictures of such 'blunders' is the Science and Technology Agency's (STA) cancellation of the patent granted for Yuzuru Fushimi's four-color fluorescent labeling in 1984, owing to the government's 'ban' on patenting the outcome of research based on public funding (in drastic contrast with the Bayh–Dole Act in the United States in 1980). A Caltech team applied for similar technology in the same month as Fushimi's patent was withdrawn (Kishi, 2004: 46–53).
2. In their original intention, 'funneling' is for describing rhetorical devices in the scientific text to direct the readers' concern from an abstract background to a specific issue. I adopt this term for describing the selection process from early expectations to its targeted policy agenda.
3. In the pre-war period, Institute of Physical and Chemical Research (RIKEN) thrived as a large financial conglomerate (*zaibatsu*), combining both basic and applied research. It engaged in activities from building accelerators to selling products such as 'RIKEN *Vitamin*' (A) and synthetic *sake* (Miyata 1983). After the Second World War, RIKEN was dissolved by the General Headquarters, surviving through that difficult time as a limited company KAKEN (acronym for the Institute of Science) from 1948 to 1958 (RIKEN, 2005).
4. Mutsu was constructed in 1968, but experienced minor nuclear leakage in 1974. The experiment was finalized in 1993. http://www.jaea.go.jp/04/aomori/nuclear-power-ship/index.html (accessed 13 May 2012).
5. Wada may be seen as an example of a 'big man' (Sleeboom-Faulkner and Patra, 2011); as Hayashi (2006) discusses in the case of Japan's genomic policy, however, this can be also interpreted as a lack of 'boundary organizations' (Guston, 2000) in Japan's landscape of science policy, necessitating that people like Wada fill the gap with his personal network.
6. Gelfert (2012) analyzes a similar exchange between Japan and the United States at the launch of the National Nanotechnology Initiative (NNI).
7. The eight hubs were covering major national universities and institutions: the Universities of Tokyo, Osaka, Kyoto, Hokkaido, and Yokomaha City as well as KEK (High Energy Accelerator Research Organizations) accelerator laboratory.
8. In some university laboratories, an escape route was invented by counting as plural the intermediate shapes of the folds within the same protein to attain the target (Interview 2). Masuda (2002) had already warned of this possibility.
9. Some of those who participated in the Human Genome Project (HGP) also raised their voices against the monopoly of funding by protein researchers, arguing that genomics still needed to be funded (Shimizu, 2000).

References

Abbott A (2005) Protein structures hint at the shape of things to come. *Nature* 435: 547.

Anonymous (1986) Kagakugijutuchô 30 nen no ayumi [30 years of Science and Technology Agency]. *Purometeusu* 52.

Anonymous (2001) Unsung heroes. *Science* 291(5507): 1207.

Anonymous (2007) Abunaizo, kagaku gijutsu rikkoku [Techno-science nation in crisis]. *Nikkei Shinbun*, 12 February, p. 19.

Anonymous (2009) Kisokara wakaru kagakugijutsu yosan [Basics of the science technology budget]. *Yomiuri Shinbun*, 10 December, p. 13.

Arata Y (2008) Jitsuzô to kyozô [Image and truth]. In: Tsukihara T and Nakamura H (eds) *Tanpaku 3000 purojekuto no unda mono* [What Protein 3000 Project has achieved]. *Tanpakushitsu*, *Kakusan*, *Kôso* 53(5): 645–647.

Arata Y (2010) *Nihon no kagaku seisaku wo tou* [Questioning Japanese Science Policy]. Tokyo: Yakuji-shinpo sha.

Bakker S, van Lente H and Meeus M (2011) Arenas of expectations for hydrogen technologies. *Technological Forecasting & Social Change* 78(1): 152–162.

Bateson G (1972) *Steps to an Ecology of Mind: Collected Essays in Anthropology, Psychiatry, Evolution and Epistemology*. New York: Ballantine Books.

Berube DM (2006) *Nano-Hype: The Truth behind the Nanotechnology Buzz*. Amherst, NY: Prometheus Books.

Blume S (2003) *Insight and Industry: On the Dynamics of Technological Change in Medicine*. Cambridge, MA: MIT Press.

Bonanno J (1999) Structural genomics. *Current Biology* 9(23): R872.

Borup M, Brown N, Konrad K and van Lente H (2006) The sociology of expectations in science and technology. *Technology Analysis & Strategic Management* 18(3–4): 285–298.

Brenner SE and Levitt M (2000) Expectations from structural genomics. *Protein Science* 9: 197–200.

Brown N (2003) Hope against hype: Accountability in biopasts, presents and futures. *Science Studies* 16(2): 3–21.

Brown N, Rappert B and Webster A (eds) (2000) *Contested Futures: A Sociology of Prospective Techno-science*. Aldershot: Ashgate.

Chee LPY and Clancey G (2013) The human proteome and the Chinese liver. *Science Technology and Society* 18(3): 307–319.

Chothia C (1992) Proteins. One thousand families for the molecular biologist. *Nature* 357(6379): 543–544.

Chouard T (2011) Structural biology: Breaking the protein rules. *Nature* 471(7337): 151–153.

Collingridge D (1992) *The Management of Scale: Big Organizations, Big Decisions, Big Mistakes*. London: Routledge.

Cook-Deegan R (1994) *The Gene Wars: Science, Politics, and the Human Genome*. New York: Norton & Company.

Cyranoski D (2006) 'Big science' protein project under fire. *Nature* 443(7110): 382.

Davies G, Frow E and Leonelli S (2013) Bigger, faster, better? Rhetorics and practices of large-scale research in contemporary bioscience. *BioSocieties* 8(4): 386–396.

De Solla Price DJ (1965) *Little Science, Big Science*. New York: Columbia University Press.

Disco C and Van Der Meulen B (eds) (1998) *Getting New Technologies Together: Studies in Making Sociotechnical Order*. Berlin: Walter de Gruyter.

Duncker E (2001) Symbolic communication in multidisciplinary cooperations. *Science, Technology & Human Values* 26(3): 349–386.

Duncker E and Disco C (1998) Meaningful boundaries: symbolic representations in heterogeneous research and development projects. In: Disco C and Van Der Meulen B (eds) *Getting New Technologies Together: Studies in Making Sociotechnical Order*. Berlin: Walter de Gruyter, pp. 265–297.

Fortun M (2008) *Promising Genomics: Iceland and deCODE Genetics in a World of Speculation*. Berkeley, CA: University of California Press.

Fujimura J (1999) The Practices of producing meaning in bioinformatics. In: Fortun M and Mendelson E (eds) *The Practice of Human Genetics*. Dortrecht: Kluwer Academic Publishers, pp. 49–87.

Fukushima M (2013) Between the laboratory and the policy process: Research, scientific community and administration in Japanese chemical biology. *East Asian Science, Technology and Society* 7(1): 7–33.

Gaasterland T (1998) Structural genomics: bioinformatics in the driver's seat. *Nature Biotechnology* 16(7): 625–627.

Galison P (1992) The many faces of big science. In: Galison P and Hevly B (eds) *Big Science: The Growth of Large-Scale Research*. Stanford, CA: Stanford University Press, pp. 1–17.

García-Sancho M (2012) *Biology, Computing and the History of Molecular Sequencing: From Proteins to DNA, 1945–2000*. Basingstoke: Palgrave Macmillan.

Gartner (2012) Hypecycles. Available at: http://www.gartner.com/technology/research/methodologies/hype-cycles.jsp#h (accessed June 11 2012).

Gelfert A (2012) Nanotechnology as ideology: Towards a critical theory of converging technologies. *Science, Technology, and Society* 17(1): 143–164.

Gershon D (2000) Structural genomics: From cottage industry to industrial revolution. *Nature* 408(6809): 273–274.

Gerstein AE, Arrowsmith C H and Monteliones GT (2003) Structural genomics: Current progress. *Science* 299(5613): 1663.

Goldstein D (1998) An unacknowledged problem for structural genomics. *Nature Biotechnology* 16(8): 696.

Guston DH (2000) *Between Politics and Science: Assuring the Integrity and Productivity of Research*. Cambridge: Cambridge University Press.

Hakozaki T (2008) Ekkususen kôzôseibutsugaku no senmonka kara [Comments on Protein 3000 from a X-ray structural biologist]. In: Tsukihara T and Nakamura H (eds) *Tanpaku 3000 purojekuto no unda mono* [What the Protein 3000 Project has achieved]. *Tanpakushitsu*, *Kakusan*, *Kôso* 53(3): 652–654.

Hayashi Y (2006) Nihon no hitogenomu keikaku ni miru nihon no kagakugijutu seisaku ketteikatei ni kansuru baikaikikô to sono kadai. [The mediating function and its problem of Japan's science policy formation seen in the Human Genome Project in Japan and the US] *Kenku, Gijutsu, Keikaku* 21(2): 202–213.

Heinemann U (2000) Structural genomics in Europe: Slow start, strong finish? *Nature Structural Biology* 7(Structural Genomics Supplement): 940–942.

Hilgartner S (2013) Constituting large-scale biology: Building a regime of governance in the early years of the Human Genome Project. *BioSocieties* 8(4): 397–416.

Hol W (2000) Structural genomics for science and society. *Nature Structural Biology* 7(Structural Genomics Supplement): 964–966.

Ikura M (2008) Kagaku to ôgatayosan: Biggu saiensu ga umidashita mono [Science and big stakes: Invisible outcomes of 'big science']. In: Tsukihara T and Nakamura H (eds) *Tanpaku 3000 purojekuto no unda mono* [What the Protein 3000 Project has achieved]. *Tanpakushitsu*, *Kakusan*, *Kôso* 53(5): 648–651.

International Structural Genomics Organization (ISGO) (2013) Homepage. Available at http://www.isgo.org (accessed 1 April 2013).

Isaji M (2009) *Kagaku purojekuto hihan no yôin: Tanpaku 3000 wo reito shite* [Reasons for criticisms of a scientific project: Protein 3000 as an example]. Unpublished Masters' Thesis, Waseda University, Tokyo, Japan.

Ito Y (2005) Science lessons: Japan must learn from its mistakes in the Human Genome Project. *Nature* 433(7022): 107–108.

Kay LE (2000) *Who Wrote the Book of Life: A History of the Genetic Code*. Stanford, CA: Stanford University Press.

Kishi N (2004) *Genomu Haiboku: Chizai Rikkoku Nihon ga Abunai!* [Defeat in the Genome: Japan's National Policy for Intellectual Property in Danger!]. Tokyo: Daiamondo-sha.

Konrad K (2006) The social dynamics of expectations: The interaction of collective and actor-specific expectations on electronic commerce and interactive television. *Technology Analysis & Strategic Management* 18(3/4): 429–444.

Law J (1986) The heterogeneity of texts. In: Callon M, Law J and Rip A (eds) *Mapping the Dynamics of Science and Technology*. London: Macmillan, pp. 67–83.

Lee F (2015) Purity and interest: On relational work and epistemic value in the biomedical sciences. In: Dussauge I, Helgesson CF and Lee F (eds) *Value Practices in the Life Sciences and Medicine*. Oxford: Oxford University Press, pp. 207–223.

Lenoir T (1997) *Instituting Science: The Cultural Production of Scientific Disciplines*. Stanford, CA: Stanford University press.

Lewis J and Bartlett A (2013) Inscribing a discipline: Tensions in the field of bioinformatics. *New Genetics and Society* 32(3): 243–263.

McGee MC (1980) The 'ideograph': A link between rhetoric and ideology. *Quarterly Journal of Speech* 66(1): 1–16.

MacKenzie A (2003) Bringing sequences to life: How bioinformatics corporealizes sequence data. *New Genetics and Society* 22(3): 315–332.

MacKenzie A, Waterton C, Ellis R, Frow EK, McNally R, Busch L, et al. (2013) Classifying, constructing, and identifying life: Standards as transformations of 'the biological'. *Science, Technology & Human Values* 38(5): 701–722.

Martin P (2002) Gene therapy: expectations and results. In: *Nature Encyclopedia of the Human Genome*. London: MacMillan Publishers Ltd., pp. 1–4.

Masuda T (2002) Kachiaru kaiseki deeta wo daseruka? [Can the research produce valuable information?] *Nikkei Biojournal* 11: 10–11.

MEXT (2007) Tanpaku 3000: Jigohyôka hôkokusho [Official Evaluation Report of Protein 3000 Project]. Available at: www.tanpaku.org/old_project/protein02a.php (accessed August 9 2008).

MEXT (2011) Targeted proteins research project. Available at: www.tanpaku.org (accessed 3 June 2011).

Meyers TC, Turano TA, Greenhalgh DA and Waller PRH (2000) Patent protection for protein structures and databases. *Nature Structural Biology* 7(Structural Genomics Supplement): 950–952.

Michael M, Wainwright S, Williams C, Farsides B and Cribb A (2007) From core set to assemblage: On the dynamics of exclusion and inclusion in the failure to derive beta cells from embryonic stem cells. *Science Studies* 20(1): 5–25.

Milne R (2012) Pharmaceutical prospects: Biopharming and the geography of technological expectations. *Social Studies of Science* 42(2): 290–306.

Miyata S (1983) *Kagakusha tachi no jiyûna rakuen* [A Free Paradise for Scientists]. Tokyo: Bungeishunju.

Montelione GT (2001) Structural genomics: An approach to the protein folding problem. *Proceedings of the National Academy of Sciences* 98(24): 13488–13489.

Morris P and Travis AS (2002) The role of physical instrumentation in structural organic chemistry in the twentieth century. In: Morris P (ed.) *From Classical to Modern Chemistry: The Instrumental Revolution*. Cambridge: The Royal Society of Chemistry, pp. 57–84.

Myers N (2008) Molecular embodiments and the body-work of modeling in protein crystallography. *Social Studies of Science* 38(2): 163–199.

Nakamura K (2007) Seimeikagaku kenkyû: Kyohi ni niau mokuteki meikaku ni [Life science research: Make clear the purpose of big budget] *Asahi-Shinbun*, 17 May, p. 15.

Oda M (1998) Maintaining science culture in Japan. *Nature* 391(6666): 431.

Oshima Y (2007) Tanpaku 3000 ga nokoshita mono [The Legacy of the Protein 3000 Project]. *Gendai kagaku* 434: 14–21.

Oshima Y, Nishimura Y, Kuramitsu S, Yokoyama S, Wakatsuki S and Nakamura H (2002a) Zadankai: Kôzô puroteomikusu ha naniwo mezasu no ka? [Round table: What does structural proteomics aim at?]. In: Oshima Y, Nishimura Y, Kuramitsu S, Yokoyama S, Wakatsuki S and Nakamura H (eds) *Kôzô puroteomikusu* [Structural Proteomics]. *Tanpakushitsu*, *Kakusan*, *Kôso* 47(8): 865–881.

Oshima Y, Nishimura Y, Yokoyama S and Nakamura H (eds) (2002b) *Kôzô puroteomikusu* [Structural Proteomics]. *Tanpakushitsu*, *Kakusan*, *Kôso* 47(8).

Parker JN, Penders B and Vermeulen N (eds) (2010) *Collaboration in the New Life Sciences*. Farnham: Ashgate.

Pellegrini L (2005) No royal road to protein structure determination. *Nature* 436(7048): 174.

Pollock N and Williams R (2010) The business of expectations: How promissory organizations shape technology and innovation. *Social Studies of Science* 40(4): 525–548.

RIKEN (2005) Riken 88 nenshi (88 Years of RIKEN's History). Available at: http://www.riken.go.jp/r-world/info/release/riken88/book/ (accessed 12 May 2012).

RIKEN (2008) RIKEN news, 21 February. Available at: http://www.riken.jp/~/media/riken/pr/topics/2008/20080221_1/20080221_1.pd (accessed 18 January 2012).

Rip A (2006) Folk theories of nanotechnologists. *Science as Culture* 15(4): 349–365.

Schrader A (2010) Responding to *Pfiesteria piscicida* (the fish killer): Phantomatic ontologies, indeterminacy and responsibility in toxic microbiology. *Social Studies of Science* 40(2): 275–306.

Service R (2002) Tapping DNA for structures produces a trickle. *Science* 298(5595): 948–950.

Shimizu N (2000) *Nihon no toppuranna Shimizu Nobuhiro ga toku hitogenomu keikaku no kyotojitsu* [The Lies and the Reality of Human Genome Project, Illuminated by Nobuyoshi Shimizu, Japan's Top Runner]. Tokyo: Bujinesu-sha.

Sleeboom-Faulkner M and Patra PK (2011) Experimental stem cell therapy: Biohierarchies and bionetworking in Japan and India. *Social Studies of Science* 41(5): 645–666.

Smaglik P (2000) Genomics initiative to decipher 10,000 protein structures. *Nature* 407(6804): 549.

Star SL and Griesemer JR (1989) Institutional ecology, 'translations' and boundary objects: Amateurs and professionals in Berkeley's Museum of Vertebrate Zoology, 1907–39. *Social Studies of Science* 79: 387–420.

Stemerding D and Hilgartner S (1998) Means of coordination in making biological science: On the mapping of plants, animals and genes. In: Disco C and Van Der Meulen B (eds) *Getting New Technologies Together: Studies in Making Sociotechnical Order*. Berlin: Walter de Gruyter, pp. 39–69.

Stevens H (2013) *Life Out of Sequence: A Data-driven History of Bioinformatics*. Chicago, IL: University of Chicago Press.

Suea SC, Chang CF, Huang YT, Chou CY and Huang TH (2005) Challenges in NMR-based structural genomics. *Physica A* 350(1): 12–27.

Swinbanks D (1996) Superconductivity spurs Japanese plan for NMR research. *Nature* 381(6578): 105.

Tasumi M (2006) Kôzô seibusugaku kotohajime [The early days of structural biology]. *Life on Proteins Newsletter* 15: 51–59.

Terwilliger TC (2000) Structural genomics in North America 2000. *Nature Structural Biology* 7(Structural Genomics Supplement): 935–939.

Traweek S (1988) *Beamtimes and Lifetimes: The World of High Energy Physicists*, Cambridge, MA: Harvard University Press.

Triendl R (2001) Staffing shortage threatens Japan's structural genomics. *Nature* 410(6829): 724.

Tsukihara T and Nakamura H (eds) (2008) *Tanpaku 3000 purojekuto no unda mono* [What Protein 3000 Project has achieved]. *Tanpakushitsu*, *Kakusan*, *Kôso* 53(5).

Tutton R (2011) Promising pessimism: Reading the futures to be avoided in biotech. *Social Studies of Science* 41(3): 411–429.

Twyman R (2004) *Principles of Proteomics*. New York: Taylor & Francis.

US Congress, Office of Technology Assessment (1988) *Mapping Our Genes-The Genome Projects: How Big, How Fast? (OTA-BA-373)*. Washington, DC: U.S. Government Printing Office).

Van Lente H (1993) *Promising Technology: The Dynamics of Expectations in Technological Developments*. Unpublished Doctoral Thesis, University of Twente, Enschede.

Van Lente H, Spitters C and Peine A (2013) Comparing technological hype cycles: Towards a theory, *Technological Forecasting & Social Change* 80: 1615–1628.

Venter J C (2007) *A Life Decoded: My Genome: My Life*. London: Allen Lane.

Venter JC, Smith HO and Leroy H (1996) A new strategy for genome sequencing. *Nature* 381(6581): 364–366.

Vermeulen N (2010) *Supersizing Science: On Building Large-Scale Research Projects in Biology*. Boca Raton, FL: Universal-Publishers.

Wada A (2005) *Butsurigaku ha ekkyô suru* [Physics Crosses Boundaries]. Tokyo: Iwanami shoten.

Wada A (2007) Tanpaku 3000 purojekuto no kiban [The basis of Protein 3000 Project]. Available at http://scienceportal.jp/news/review/36614/20070518.html (accessed 23 May 2012).

Wada A (2008) *Seimeitoha? Busshituka!* [What is life? The Matter!]. Tokyo: Ômusha.

Wada A, Yamamoto M and Soeda E (1983) Automatic DNA sequencer: Computer programmed microchemical manipulator for the Maxam–Gilbert sequencing method. *Review of Scientific Instruments* 54(11): 1569.

Watanabe Memorial Foundation (ed.) (2009) *Kagaku-gijutsuchô seisaku shi: Sono seiritsu to hatten* [The history of science policy of Science and Technology Agency: Form its foundation to its Development]. Tokyo: Kagaku-Shinbun Sha.

Williams R (2006) Compressed foresight and narrative bias: Pitfalls in assessing high technology futures. *Science as Culture* 15(4): 327–348.

Wüthrich K (1986) *NMR of Proteins and Nucleic Acids*. New York: Wiley-Interscience.

Yanagita M, Ikura M, Morikawa K, Nanba K, Inagaki F and Nishimura Y (1999) Zadankai-Kôzô seibutsugaku ha nani wo mezasunoka [Round talk: What does structural biology aim at?]. In: Nishimura Y, Kyogoku Y, Itagaki F and Morikawa K (eds) *Kôzôseibutsugaku no furontia* [The Frontier of Structural Biology] (*Tanpakushitsu*, *Kakusan*, *Koso*, special issue): 614–629.

Yokoyama S, Hirota H, Kigawa T, Yabuki T, Shirouzu M, Terada T, et al. (2000a) Structural genomics projects in Japan, *Nature Structural Biology* 7(Structural Genomics Supplement): 943–945.

Yokoyama S, Matsuo Y, Hirota H, Kigawa T, Shirouzu M, Kuroda Y, et al. (2000b) Review: Structural genomics projects in Japan, *Progress in Biophysics & Molecular Biology* 73(5): 363–376.

Yokoyama S, Terwilliger TC, Kuramitsu S, Moras D and Sussman JL (2007) RIKEN aids international structural genomics efforts, *Nature* 445(7123): 21.

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