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From brainbank to database: the informational turn in the study of the brain

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Abstract

Brain in a vat scenarios in analytic philosophy feature both brains and technological apparatus. The relation between specimens and technology is an interesting aspect of these scenarios, and in order to explore this relation, I contrast here two kinds of scientific collecting practices: the collection of post-mortem brains versus the compilation of digital brain atlases. This contrast highlights a novel configuration of the relation between brains (in digital media) and new information technologies. This new configuration is traced back to the late 1980s, which saw the rise of a new kind of collection of brains, with a markedly different scope and nature: the neuroscience database. Brains are now easily captured *in vivo*, so that while post-mortem brains were precious and few, scanners provide an embarrassment of riches in the form of terabytes of data. The rise of the virtual brain as a new digital object for research is reliant on the development of new imaging technologies, but also on the growth of computerised tools, informatics, and electronic networks in this field. These developments contribute to an informational turn in scientific research. This article considers what is involved in the shift in type of object, from the scarce, wet, biological brain to a plentiful, digital, virtual one. It discusses the significance of this new object in terms of collections, institutions, and research practices.

Keywords: History of neuroscience; Neuroinformatics; Biobanks; Neuroethics; Brain imaging

1. Introduction

The 'brain in the vat' has been an important object for cognitive science and philosophy of mind. It has been the main character in countless science fiction

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narratives, and the focus of thought experiments about the relationship between the mind and the world. In its basic form, the fantasy of the brain in the vat involves two terms and their interface. First, there is a brain, as a solid, singular object. Second, there also needs to be a technological apparatus that sustains the input/output of the brain in the vat. The interface between these take place in a vat—a wet, yet non-biological milieu. This vat is usually to be found in a lab, a secret chamber ceremoniously visited (and sometimes violated), where the engineered interface between the mental and the material takes place. In the philosopher Daniel Dennett's essay 'Where am I?',[1] the fantasy also involves the possibility of transferring the content of the mind to a computer. Such scenarios raise questions about the relations between consciousness, identity, and embodiment.

These narratives are framed within a very specific kind of American cognitive science, in which the notion of *function* dominates the formulation and resolution of issues of location, identity, and embodiment. If the functional patterns of mind can be emulated, then information processing transcends the material substrate. This view has been conveyed in the metaphor 'the mind as software', used to delineate the domain of cognitive science. The metaphor excludes the brain as essential physical substrate: the platform running the software doesn't really make a difference to the program. If the brain's contents could be properly interfaced and downloaded (the perfect brain in the vat setup), the study of mind could proceed unencumbered. Over the past decade, many researchers have rejected the metaphor, in favour of an integrated approach—looking at both 'software' and 'hardware'.[2] The sciences of mind have therefore taken a biological turn, while continuing to embrace the possibilities of computational approaches. The wet brain of cognitive neuroscience is incorporated into the technological and informational science via translation into the digital realm, rather than through excision from the body and connection to an apparatus.

The tension between the wet brain and information and communication technology (ICT) has therefore developed another configuration: the material itself becomes informationalised. In cognitive neuroscience, a digital rendition of anatomy is now used to map the brain's function. The emphasis on the biological materiality of the mind in this field therefore relies, somewhat paradoxically, on the virtual brain. Through this configuration, where materiality and virtuality reinforce each other, wet biological materials join the study of mind in a digital context, and an important link is established between neuroscience, the biomedical sciences and the sciences of mind.

In this new context, it makes sense to talk about 'having information for every voxel in the brain', as though voxels, which are units of information in a 3D space,

[1] This text gave rise to a number of reactions, some of them collected in Dennett (1981).

[2] See for example Kosslyn & Koenig (1992), who describe the shift as 'doing wet mind'. The various stages of Kosslyn's research illustrate this shift, from a functional approach to one where the brain is used to 'constrain' cognitive theories.

are to be found in the brain. This shift in the tension between the material and the informational, its assumptions, and consequences, are discussed in this article.

2. Informational turn

The virtual brain, located in databases and in networks of technologies, constitutes a new territory for the study of the brain and mind. A new set of research practices, in which information and information technologies play a crucial role, is associated with this version of the brain.[3] In this article, I will contrast 'wet' and 'virtual' brains as epistemic objects within experimental systems (Rheinberger, 1997). Epistemic objects are at the centre of scientific research practice, and are continually materially redefined to yield interesting results. The analysis that follows treats these objects as templates, each serving to characterize the particularities of the other. The hope is that this will highlight assumptions that might otherwise remain invisible. For example, the wet brain in the pathological lab will serve as both a contrast to and a reminder of the physicality of scientific objects (including digital ones), while the explicit requirements for anatomical study of the brain in each kind of collection show how priorities contrast, in relation to the features of the materials each collection contains.[4]

In addition to highlighting historical changes in the neurosciences, this article hopes to contribute to an analytic framework for understanding the 'informational turn'[5] in a number of areas of scientific research. The contours of this shift are only beginning to be sketched in fields of communication, science and technology studies, and history of science. Two significant elements arise from the work to date and inform the study of the informational turn. The first relates to the need to consider the interactions between technologies, rather than single tools (the PC) or applications (email) (Hagen, 2001; Hine, 2000; Nardi & O'Day, 1999). The second element is the importance of the interaction between the deployment of technologies, and the knowledge being produced and its uses (Bowker & Star, 1999; Lenoir, 1998; Robins &

[3] I will avoid here the expression 'computational neuroanatomy' to denote this field, as there are different types of work being subsumed under this label. The term generally refers to the development of methods for studying brain shape among different populations (the work pursued by Thompson and colleagues at UCLA and by Ashburner and colleagues at the FIL, UCL London). It is also used as a label for the inclusion of neuroanatomy into computational models (i.e. providing 'neuroanatomical realism' to neural networks). There are bridges between these bodies of work (for example Bjaalie, 2001) but they generally have different research traditions, settings, and objects.

[4] Of course, what makes the juxtaposition interesting is that they are 'about' the same thing: the brain. Hopefully this can stand without too much of a reliance on a realist notion of what the brain might be. I address this issue indirectly, by showing how the two approaches to the study of neuroanatomy overlap and interact.

[5] Wouters (2002); Wouters, Beaulieu, Park, & Scharhorst (2002). The notion of 'turn' indicates that important transformations are taking place, but because we do not assume that the sciences will change in every respect, we do not speak of an informational revolution. The work of Hine on a public forum of informal scientific communication also indicates that changes are likely to be partial and gradual rather than radical (Hine, 2002).

Webster, 1999). Indeed, the very issue of what can be known is raised by new research practices. Work on the biological sciences, where the informational turn has been especially sharp (Kay, 2000), shows how the disciplinary aspirations and the very epistemics of a field change as new research practices reliant on information and communication technologies are integrated (Bowker, 2000; Hagen, 2001; Lenoir, 1998).

Besides taking these interactions into account, our framework to study the informational turn focuses on two main dynamics: the role of digital information and the networked character of research (Wouters et al., 2002). With regard to the production of digital information, the role of new technologies is especially visible. The use of these new tools often means that data production becomes quantified, automated, or both. This may in turn lead to the creation of databases and other repositories, and to new types of experiments. This dynamic around digital information is neither inevitable nor identical across the sciences, but it is recognisable. For example, advances in visualisation, databasing, hardware networking, and automation all played a role in making (some parts of) biomedicine informational (Lenoir, 1998). These changes are sometimes said to lead to 'data floods', and be followed by calls for yet more tools and infrastructures to manage these developments. Studying this dynamic may be a useful way to address challenges to current scientific practices. To give but one example, the growing amount of digital data ('data floods'), and a growing trend towards sharing data may also affect crucial processes of quality control in science, such as peer-review (Wouters & Beaulieu, 2002).

The second related dynamic is the increasingly networked organisation of science, which can be observed in various aspects of research. With regard to the development of research questions, interdisciplinary research, organised around specific problems, is increasingly prominent. Developments in neighbouring fields can also create new links in such networks, as new data repositories or tools become available. The field of taxonomy, for example, embraced bioinformatics via genetics (especially the availability of sequencing data) (Hagen, 2001).

Not only the research agendas but also the physical place of science may take on a networked character. The laboratory, for example, may be challenged as the exclusive or dominant site of knowledge production, as databases (Lenoir, 2002), electronic discussion lists (Hine, 2002), or web sites (Beaulieu & Simakova, 2002) come to fulfil functions that were traditionally located in the lab, or as new practices arise that are distributed in many sites by their very design ('collaboratories') (Finholt, 2002). Communication in science may also rely increasingly on networks mediated by information and communication technologies. Journals may no longer be the primary site for communication about ongoing work or for the dissemination and preservation of findings (Bowker, 2000).[6] They may also become so closely entwined with data repositories as to be no longer recognisable as traditional journals (Lenoir, 2002). Finally, these various networks may interact, with

[6] The use of ICT for science communication raises new questions for science policy. Recent developments in 'webometrics' and the use of the internet to monitor scientific practices can be found at http://www.wiserweb.org/.

unanticipated consequences. Data-sharing via databases may interfere with publication practices, and distributed computation in biomedical informatics may play havoc with traditional ethical guidelines for patient protection (Wouters & Schroeder, 2003). The implications of the informational turn in science are potentially very significant. Understanding these far-reaching changes requires a focus on the two main dynamics of the informational turn: digital information and networks.

Both digital objects and networked research are increasingly present in the study of the brain, and especially in one of the areas examined in this paper, cognitive neuroscience.[7] In what follows I trace the growing presence of the brain as an informational object, by contrasting it to the brain as a wet object, and by comparing the experimental systems around these objects. This analysis will help understand how the relations between brain and technology in the study of the mind have developed into a new configuration, and how this contrasts with the classic brain in the vat scenario.

3. The materiality of research materials

Although specimens and brain tissues served as key materials of investigation for researchers since the end of the nineteenth century, the latter half of the twentieth century saw the development of large collections of brains as a particular kind of resource for research, often known simply as 'brain banks'. These have grown from small, local collections usually located in neuropathology labs, into full-fledged, often 'national' brain banks. Most existing repositories were established in the 1970s and 1980s. New banks still emerge from time to time,[8] but the main developments in the field currently focus on the coordination of activities and standards used by existing brain banks, and on the networking of brain banks at national or continental level.[9]

Even as brain banks and other collections were in an important phase of consolidation and professionalisation in the course of the 1980s, a new object for the study of the brain arose, in the form of collections of brain scans.[10] The possibility of scanning brains *in vivo* had an important impact on anatomical knowledge about the brain, providing new information and new representations of the brain. These developments are often characterized as a turning point in neuroanatomy (Damasio, 1995). Specifically, computerised tomography, which enables three-dimensional

[7] The institutional and science policy aspects are not discussed here. In the case of neuroinformatics, the funding opportunities offered by the Human Brain Project (a US federal multi-agency funding programme, 1994–2003) were especially significant.

[8] The Brisbane Brain Bank was founded in March 1994 at the Mater Hospital Pathology Laboratory, Australia; The UK Multiple Sclerosis Tissue Bank was founded by MS society in 1998, after changes in orientation in funding (it formerly funded two banks, and had less involvement).

[9] There is a North American network, as well as a European one. See n.16.

[10] Biobanks in general have been growing in scale, raising important new ethical and social issues. See Cambon-Thomsen, La bioethique a l'échelle de la biobanqu-omique. http://www.ircm.qc.ca/bioethique/obsgenetique/cadrages/cadr2003/c_no10_03/ci_no10_03_2.html.

images to be rendered, has been very important for anatomy. In this article, I want to focus more specifically on the object of research derived from *collections* of scans (brain databases), rather than on the possibilities offered by scanners and specific scans.

The constitution of collections of brains, wet or virtual, begins with seeking and obtaining 'brains'. This process is radically different in the two settings, in terms of the difficulty, the social interactions and the institutions involved. Most striking perhaps is the way researchers in both settings struggle with opposing problems: scarcity versus data floods. I begin by contrasting here the process of obtaining materials, the actors involved and the features that make these brains valuable research objects.

4. Brains for brain banks

Repositories of preserved human organs, or collections containing anatomical material, date back at least to the seventeenth century (Gere, 2003). This 350 year old history can be seen as a succession of diverse periods, marked by different rationales for collecting tissues, and changing relationships to scientific research and education (Gere, 2003). Researchers currently operating and using brain banks place the origin of brain tissue collections in practices of post-mortem examination of asylum patients. For example, these were pursued in institutions in and around London in the late nineteenth century (Davies, Everall, & Lantos, 1993). This was not unique to the British context: brain tissue was collected and preserved in at least eight countries[11] in the last decade of the nineteenth century (Davies et al., 1993). Modern brain banks, characterised by increasingly sophisticated and reliable cryosection techniques, date from the 1960s. Wallace Tourtelotte is credited with the initiation of collection and preservation in the US, while E. D. Bird developed the first collection of tissue (from patients with Huntington's Disease) in the UK in 1971, later moving to Boston in 1974, where this collection has grown to be one of the largest in the world (Cruz-Sanchez & Tolosa, 1993).[12] Patients and patient organizations were also involved in some of these early efforts, though their involvement became more structural as patient organizations professionalized in the 1980s and 1990s.[13] In turn, brain banks also started to pay more attention to patient organizations as loci for recruitment of donors (Gere, 2003).

Most brain banks were developed by clinicians and neuropathologists, due to their proximity to tissues (Cruz-Sanchez & Tolosa, 1993). These were obtained as part of their research activities in labs and departments. The banks, however, differ from the labs in a number of important ways. Material from neuro-pathological

[11] The countries are Germany, France, Holland, Italy, Norway, Portugal, Russia, and Switzerland.

[12] See 'Ethical issues in brain banking', http://www.iprs.it/brainelsa/BACKUP_cd/banks1-1ter.htm.

[13] Some brain banks are sponsored and even administered by patient organisations, such as the MS brain bank, Imperial College, London, UK, sponsored by the UK MS Society.

laboratories or clinical and basic laboratories was collected for diagnosis or specific studies (Cruz-Sanchez & Tolosa, 1993). In a brain bank, this material tends to be more organised and more public, and oriented to serving larger communities of researchers. A brain bank also differs from a neuropathology lab's collection, in that in that it usually has explicit protocols for collection and in that gathers some basic information for all the brains in its collections, so that specimens are documented in a standardized manner. Indeed, issues of standardisation, in both dissection of brains and cryopreservation, were the topics of a series of major conferences in 1979, 1980, and 1982 (Cruz-Sanchez & Tolosa, 1993). More recently, neuroscientists have established elaborate schemes for collecting, classifying, and sharing brain tissues, for example through the European 'EURAGE' organization coordinating research on aging and dementia (Prins, 1998).

While brain banks are more multi-disciplinarily oriented, the tie with neuropathology persists. For example, some brain banks offer families of donors a neuropathological report, retaining the diagnostic tradition in relation to tissue samples. A further contrast with neuropathological collection, however, emerges with the gathering of brains of people who had *not* been diagnosed with a particular brain condition—these non-pathological samples are called 'controls', and serve as contrasts to diseased tissues. As objects, brains are variously dissected, sliced, and preserved by being frozen or fixed. A common practice has been to select one hemisphere for dissection and to preserve the other, alternating which hemisphere receives which treatment in a random way. This splitting up of the brain tissues contrasts, as I will show, with the whole brain approach of brain databases.

5. The scarcity of brains

The brain bank's connections to clinical science are not simply a historical residue. Indeed, the offer of a 'diagnostic' report to the family is one of the ways in which brain banks negotiate the difficult process of obtaining brains for their collections. Obtaining bodies has largely been a difficult endeavour in Western culture (Sappol, 1997). The removal of brains after death remains a delicate process.[14] The process of obtaining consent preoccupies researchers and administrators of brain banks; the need to communicate, in life with possible donors, and at the time of death with the next of kin, constitutes a persistent challenge for brain banks. A number of contexts and actors shape this communication. Professional jurisdictions and areas of competence constitute some of the main factors affecting access to brains. Historian and sociologist of Alzheimer's Ad Prins has shown that different understandings between, for example, nursing home physicians and brain bank researchers need to be bridged for collaboration to take place (Prins, 1998). Furthermore, depending on the goals of the bank, the context will be more or less local (this is discussed below), and may be more or less mediated (Swaab,

[14] The need for 'good contacts' for getting brains, and the importance of lay/family/patient organisations are stressed again and again. For example, in McPherson, Smith-Lovin, & Cook (2001).

Hauw, Reynolds, & Sorbi, 1989). In the American context, the medical examiner is a key actor.

6. What makes a good wet brain?

Beyond the scarcity of brains, certain features make them especially valuable to the brain banks. Certain banks are oriented to specific pathologies. In these cases, a clear diagnosis for that condition is an important factor. Furthermore, the issue of documentation seems to be a dominant concern: basic information must be known about the donor for the tissue to be deemed usable. This usually includes basic demographics, information about life course and any possible illnesses, state of health at the time of death, and further details about how the brain was obtained and prepared. In terms of the quality of collections, size is sometimes emphasised, while other banks pursue strategies to make the samples in their collections as uniform as possible. For example, the Netherlands Brain Bank (NBB) has two unique features: human brain tissue is obtained very quickly after death (2–6 hours) and the brain is dissected in a 'fresh' state (rather than fixed or cryosectioned), which allows more techniques to be used to investigate these tissues.[15] Other brain banks have a wider window (within 24 hours of death), and accept tissues removed obtained via a variety of sources—organ donation banks, medical examiners, morticians, and so on (Abdulla, 1999).

The documentation of brains can also be a factor in efficient access to the collection. The NBB, as well as a number of other banks, increasingly make use of standardised reports about the donors and brains, so that requesting tissues becomes easier for researchers using the brain banks. Indeed, calls for standardisation have been heard in many settings and are one of the main agenda items for the various networks of brain banks that have developed recently.[16] Standardisation of protocols for dissection and brain preparation, of diagnosis, and of information available for brain collections are current priorities.

7. Brains for databases

If academic neuropathology departments are at the origin of most brain banks, the institutions that build and manage brain databases are more diverse. Some are established academic neuroscience departments, while other have links to clinical settings. A number of databases are also maintained under the aegis of national

[15] This material is taken from http://www.brainbank.nl/nhb/engels/hb_index_eng.htm, 14 January 2003.

[16] There is the American Network of Brain Banks, and the European Brain Banks Network, established under grant 'European Brain Bank Network for neurobiological studies in neurological and psychiatric disorders' (EBBN), for the period 1993–1996, in the BIOMED-1 programme of the European Community.

scientific organisation, and are meant to function as community resources. This diversity is due to the early development of scanners, which involved a number of specialties (Beaulieu, 2002; Blume, 1992; Kevles, 1997), and the involvement of informaticians, computer scientists and mathematicians in the development of tools to archive scans.

Whereas obtaining a wet brain is difficult, acquiring brain images via scanners is rather less problematic. The procedure is regulated by ethical conventions regarding research on human subjects (including the usual informed consent). The participation of subjects in experiments is much valued by researchers, who go to great lengths to motivate and discipline their subjects, especially in the well-known brain mapping experiments (Roepstorff, 2002). Subjects, however, approach the issue of participating in a brain database in a radically different way than brain donors. Whereas donating one's brain is a selfless deed, done for the greater good, to benefit one's fellow patients or 'humankind', obtaining digital brains is generally relatively easy and the source of personal, individual pleasure.

A recent ethnographic study of participants in functional imaging research found that participants had feelings of awe and enchantment at the sight of their brain scans, given to them as either printouts on paper, or as a file on CD-ROM (Bichard, 2002). Indeed, obtaining a scan is one of the motivations (and one of the promised rewards) for participating in a study. The making of a scan is understood by subjects as a self-revelatory event, and the enchantment subjects feel looking at their scans is related to self-discovery, the sense that 'this is me, really me' (Bichard, 2002). With the proper kind of 'slice' (and indeed, the kind of slices provided to subjects usually include a 'profile' view), the family nose with its recognisable bump is outlined on the scan. The personal becomes techno-scientific, and vice versa, a translation that has become culturally resonant (Dumit, 1998) and institutionally supported (Beaulieu, 2003). The inscription of the self onto a screen, onto a digitised image, provides a particular kind of pleasure and sustains a very different economy of gift-giving than in the case of brain bank donations. The conflation of the embodied/personal and the technological/impersonal produces an interpolation, a recognition of oneself as being involved in a public event, that may seem either threatening or pleasurable, depending on the kind of control and purpose of the images that is perceived.[17] The contemplation of the self on screen is pleasurable, in a way that the contemplation of one's post mortem archived brain is not. In Dennet's 'Where am I?', the question about the location of the self arises first as the post-surgical platitude, to which the answer is easily provided as the geographical location of the waking patient. The question is exploded,

[17] For example, an obstetric ultrasound can be a pleasurable intimate object (baby's first picture), or it can be perceived as enrolment in a biomedical system of surveillance—or be both more or less at the same time. Similar fascination can be noted in the craze for 'x-ray' portraits of bejewelled ladies' hands in the early days of this technology, or in the fact that a satellite image brokering company like World-Sat finds that most demand comes from people wanting satellite images of their own homes (Garfinkel, 2000). A close reading of the particular dimensions of these pleasures would tell a fascinating story of the relation between self and technology.

however, when the narrator contemplates his brain in the vat and reflects on the consequences of dislocation and multi-location of his material body and functioning self/selves:

> Being a philosopher of firm physicalist conviction, I believed unswervingly that the tokening of my thoughts was occurring somewhere in my brain: yet, when I thought 'Here I am,' where the thought occurred to me was *here*, outside the vat, where I, Dennett, was standing staring at my brain ... I tried and tried to think myself into the vat, but to no avail. I tried to build up to the task by doing mental exercises. ... 'Here in Houston' worked well enough, and so did 'here in the lab,' and even 'here in this part of the lab,' but 'here in the vat' always seemed merely an unmeant mental mouthing. I tried closing my eyes while thinking it. This seemed to help, but still I couldn't manage to pull it off, except perhaps for a fleeting instant. I couldn't be sure. The discovery that I couldn't be sure was also unsettling. How did I know *where* I meant by 'here' when I thought 'here'? Could I *think* I meant one place when in fact I meant another? I didn't see how that could be admitted without untying the few bonds of intimacy between a person and his own mental life that had survived the onslaught of the brain scientists and philosophers, the physicalists and behaviorists. Perhaps I was incorrigible about where I *meant* when I said 'here'.[18]

Issues of identity are also at play in the larger, collective sense of *human* identity. It is interesting to note that although the two kinds of collections discussed here differ markedly, both collections of scans and of brains focus on the human content of the collections as a key part of their value. The argument made is that while some animal models exist and may be useful, they are never exactly the same as human diseases. Human brains are therefore unique resources, needed to understand fully diseases such as Alzheimer's or multiple sclerosis. Collections of wet brains align their objects of study with the uniqueness of human pathologies. Collections of scans similarly emphasise the uniqueness of humans, in relation to the cognitive–functional abilities of humans—the study of the brain in relation to language or some forms of memory can only be pursued, the argument goes, in living, functioning human brains, which can be accessed by scanning technologies. Digital scans are therefore argued to convey even more of the humanity of the brain, since it presents the brain *in vivo*, in its functional state.

8. What makes a good virtual brain?

If a key issue with post-mortem brain specimens is the need to obtain enough information (about the patients/individuals from whom they were removed, about the conditions of death, autopsy, and preservation), the handling of new collections

[18] From Dennett (1981) http://philosophy.tamucc.edu/courses/02-fall/berkich/philosophy_of_psychology_berkich/readings/dennett-where_am_i.html.

of brains poses the opposite problem of an overwhelming wealth of data. A collection of scans quickly becomes an informatics challenge, and brain imaging has been identified by the computing industry as a field where interesting challenges arise, both in terms of data management and visualisation needs. Computer science experts are therefore part of the teams that investigate brains using databases, and brain imaging is one of the main fields in which neuroinformatics is developing. Removing noise, ensuring that subjects do not move their bodies while in the scanner, recognizing artefacts due to differences in scanners, and ensuring that the various algorithms can handle all human biological variations, are all new challenges that must be met to ensure the quality of the brain as informational object of study.

Another important aspect of the virtual brain is that it becomes valuable in relation to all samples in the collection. A scan of the brain is not precious in and of itself, but becomes an interesting object by virtue of being incorporated into a database of scans, to which it can be compared and against which it can be evaluated. The possibility of comparing these objects is carefully constructed, and this possibility relies on the use of a reference space.

Scans of the brain are placed in an abstract, Cartesian space with x, y, z coordinates (see Fig. 1). Each point is labelled and can be identified numerically. Within this abstract space, data from many scans and from many subjects can be organised, and this data can then be compared and their differences measured. While there are many issues of standards, compatibility, and priorities that must be addressed to make this an effective approach to scientific data, the application of this principle marks an important conceptual shift towards the translation of objects into digital information. Once placed in a Cartesian space, the anatomy of the brain can be manipulated in terms of voxels, a set of numerical values placed in a matrix, opening the door to a wide range of manipulations, whether mathematical or statistical—and in any case, automated. In this context, the

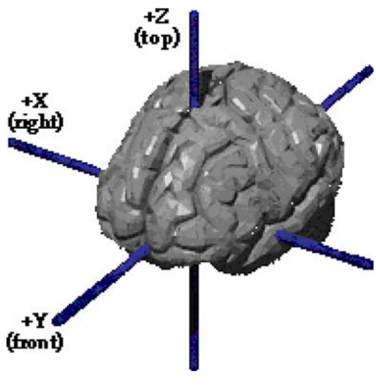

Fig. 1. The brain with Talairach axes (reproduced with the permission of the Research Imaging Center at the University of Texas Health Science Center at San Antonio).

traditional anatomy of the brain, as a landscape that is linguistically ordered, gives way to anatomy within a quantitatively ordered spatial framework. The labelling of areas in the brain, with anatomical names based on various nomenclatures (such as NeuroNames or Nomina Anatomica), gives way to coordinate systems which designate areas in the brain with numerical addresses. The space in which researchers are working therefore ceases to be a landscape to be recognised and linguistically ordered by observers, and shifts to a Euclidian, mathematized one, which can be labelled and processed automatically.[19]

Disciplinary orientations also play an important role in shaping the virtual brain. The orientation of collections of scans towards normal brains has its origin in cognitive psychology (rather than pathology), where representativity (and generalizability of findings to the general population) is an important goal. This is because cognitive and neuropsychologists and neuroscientists want to say something about the brain 'in general'. Subjects are therefore carefully selected for being part of certain populations, and the majority of collections are of healthy subjects. In this stream of research, the notion of an 'average brain' has been used as the standard for a representative brain.[20] By placing a large number of scans into a reference space, they can be 'averaged', so as to mathematically and automatically produce an average brain. Within this framework, the single scan is to be analysed in terms of the collection, and the virtual brain that is studied only exists in terms of aggregates and features of statistical significance.

The representations produced by manipulation of these collections of scans are often called atlases. The metaphor of the map, invoked by the term atlas, helps concretise what are highly abstract manipulations of data into an endeavour of surveying and exploration. They help make tangible the virtual object of research as a totalising exploration of a territory. Finally, the map is an effective metaphor for the coordination of systems of knowledge on which atlases rely, while naturalising them as features of the territory of the brain (Beaulieu, 2003).

Databases and informatics further hold the promise of searchability and easy access. These possibilities, however, will not be realised without affecting practices of researchers:

> Rapid progress towards these objectives will require increasing contributions from the arena of neuroinformatics, akin to the growing role of bioinformatics

[19] Anatomical names are also used by researchers who develop atlases, but to some extent, the referent to which various nomenclatures are translated is the coordinate system.

[20] The processes that led to this outcome are too complex to discuss here, but are detailed in Beaulieu (2001). This piece also discusses the many other brain models that have joined the average brain since the early nineties, and which often raise an eyebrow when mentioned. The idea that something so individual as a brain might be averaged, or treated mathematically, is disconcerting for some, an echo of Galton's average photographs of criminals, Jews, and army officers. Indeed, there are many assumptions about identity and normality built into these averaging procedures, which in turn are informed by ideals of objectivity. For a discussion of the use of the typical, the characteristic, and the ideal as strategies of objectivity in atlases, see Daston & Galison (1992).

> in other areas of biology. It will also require major sociological shifts in attitudes towards data sharing. (Van Essen, 2002, p. 577)

New skills and new relations of exchange will need to be configured, if these networks are to work among researchers.

Integration across disciplines is also part of the agenda. A space defined by a coordinate system can serve as a standard space within which to organise not only data from many subjects, but also from different disciplines that consider the brain on a number of scales:

> Given the importance of spatial information, brain atlases are natural gateways for navigating and visualising a wide range of neuroscientific data. Atlases provide a common spatial framework that compensates for individual differences in brain structures. When linked to suitable databases, atlases can mediate access to what is known about the brain and can lead to new insights through meta-analyses carried out on diverse data sets. (Van Essen, 2002, p. 574)

The collection of brain scans therefore cumulates functions, in a way that the collection of specimens cannot. It is also interesting to note how the reference space has become reified and naturalised. As an informational object, the virtual brain lends itself to different sets of manipulations that extend, refine, and dissolve its individual components. The original scan is both lost and extended in this series of transformations. Collections of virtual brains therefore seem to have a particular combination of functions, as data, experimental system, and model. Researchers grapple with the hybrid status of their atlases, and are often at a loss to name this beast, which is at once an atlas, a database, a summary of data and an object for further research. I return to the issue of penetration of technology and blurring of distinctions in the conclusion. To further characterise the informational turn, however, I continue with the analysis contrasting the wet and virtual brain using the category of the experimental system.

9. Investigating difference

Collections of wet and digital brains yield different possibilities for experimenting and discovering. The study of anatomical variability can illustrate these differences. The variability of the human cortex is a line of enquiry that has become closely entwined with collections of scans. The variability of size, shape and relative organisation of the brain was considered a hindrance, almost an intractable issue in the study of cerebral anatomy (Crick & Jones, 1993). It was known to exist generally, but was unknown in its particularities, in the sense of ‘not measured precisely’ (Galaburda, Leay, Kemper, & Geschwind, 1978). Brains were known to differ between individuals, especially in terms of hemispheric specialisation and in relation to handedness. This knowledge was based on neuropsychological testing and post-mortem examination of stroke and surgery patients. But after the search for the visible markers of intelligence and racial differences fell out of favour (Gere, 2003), individual differences between humans were not particularly a subject of anatomical research, though some cross-species investigations were undertaken. Prior to the development of scanning, variability seems to have been more of a burning issue in clinical settings: neurosurgeons, faced with the need to operate on one specific brain, saw the need to adapt their knowledge of anatomy to the particular patient's brain before them to avoid damaging areas important for memory or language function.

The issue of variability, however, came to occupy a much more important place when the manipulation of large numbers of scans became possible in what was to become cognitive neuroscience. Different types of digital atlases, effectively collections of scans put into a standard space, developed from the late eighties onwards. What began as a search for a better anatomical baseline to evaluate functional scans (in other words, correlating function and structure), became an important line of research.[21] Indeed, the possibility of linking variability of the brain's structure to functional variability was also increasingly explicitly articulated:

> ... variability in gyral and sulcal patterns—as anatomically distinct as fingerprints—may not present so much an obstacle as a means of distinguishing neural profiles pertinent to interindividual differences in cognitive, motor and perceptual capacities. (Jouandet et al., 1989, p. 88)

With the help of scanning and the manipulation of digital format, research into the topic of individual structural differences became 'doable' (Fujimura, 1987). Earlier researchers had used data from the archived brains of multiple subjects to make representations of different areas of the brain,[22] but the collation of data performed with collections of scans was markedly different in two respects. First, the scale upon which data can be integrated makes these digital atlases quite distinctive. Second, the use of digital technologies also shifted the kind of authority of these collations of data, from knowledge distilled in the expert's mind, to the product of complex mechanisation and automation. The sensitive topic of the relation between individual variations in function and variations in cortical structures could more easily be broached when supported by *in vivo* scanning applications and the sophisticated informatics armamentarium. The study of variability is now a well-established stream in neuroanatomy:

> Cortical variability is a research topic in itself, as it presumably accounts for many of the differences in behaviour that define human individuality. Variability is therefore one of the factors that have motivated the establishment of probabilistic human brain atlases that are based on large populations of subjects. (Bjaalie, 2002 p. 324)

[21] See computational anatomy, n. 3.

[22] Korbinian Brodmann's used data from a handful of subjects to compose his famous map, as did nineteenth century localisationists (Star, 1989).

This quotation stresses the solidity of this new research topic. Such solidity is retrospective, however, and the experimental system did not precede the production of brain atlases. Rather, it evolved along with the new epistemic object of the collection of brain scans, which was manipulated to reveal variability in increasingly sophisticated ways. In further developments of these atlases, it became possible not only to make an image of variability of the brain, but also to determine normal ranges of variability. Such a map is best rendered digitally rather than on paper, and can be viewed at http://www.loni.ucla.edu/~thompson/SZ/schizo_atlas.html. Data points are gathered into 'clouds'. Each cloud represents calculations of the various positions of anatomical structures in the brain of a normal sample. Colours are used to indicate variability, with increasingly variable areas shown in increasingly 'hot' colours. The following is a description of a map in three dimensions of normal variability in the brain:

> This map represents the magnitude and principal directions of neuroanatomical variability in normal populations (pink brain areas, highest variability, blue areas, little variability). These probability clouds are computed from shape transformations. The resulting probabilistic model of the human cortex can be used to determine whether anatomical variants in a patient are within the normal range.[23]

These atlases are called 'probabilistic' because they provide information about the probability of location of anatomical structures. These representations of anatomy therefore act as representations of what normal data might be, but also serve as sets of data that can further be explored in terms of variation. The distinction between experiment and object is not the traditional one of substance and manipulation. In informational neuroscience, this distinction is to be found in the stability of certain representations, which will serve as baselines or standards, versus the more precarious or tentative status of other representations.

10. Alzheimer's and brain collections

Research on Alzheimer's disease is a good case to highlight the particularities of research done on the virtual brain in contrast to that done on brain tissues. It also further illustrates how the experimental systems differ in terms of their relationship to clinical settings. Neuropathology, as a profession and a clinical science, focused much attention on 'diagnosis' of Alzheimer's and on the value of plaques and tangles as the hard evidence on which to base a definition of this condition (Prins, 1998).[24] The offer of diagnostic neuropathological reports from some brain banks to the families of donors is linked to the notion that neuropathological evidence is

[23] http://www.loni.ucla.edu/~thompson/SZ/schizo_atlas.html, 29 January 2003.

[24] See especially Chapter 3, 'Lumpers and splitters: cells statistics and the definition of disease' (Prins, 1998, pp. 79–123).

essential to the confirmation of a diagnosis of Alzheimer's. Presenting this state of affairs in relation to the Dutch context, Prins explains that:

> In the vocabulary of Alzheimer's disease, the clinical diagnosis and neuropathological confirmation are presented as an unambiguous stream of activities. To classify a patient properly as someone suffering from Alzheimer's disease required neuropathological investigations, restricted to the deceased ... (Prins, 1998, p. 193)

Indeed, from the neuropathological perspective, this level of evidence was so crucial that in the early period of attempts to image the particularities of Alzheimer's disease, this work using scanners was sometimes received as 'a breach of the neuropathological jurisdiction as the final answer in diagnosis'.[25] I will not further address the professional struggles about competence and jurisdiction but rather contrast the objects (these struggles should not be forgotten however, though they here remain in the background).

Collections of scans have been used to research Alzheimer's disease in the brain. This research resembles the work on variability: while it was known that the structure of the cortex seems altered in Alzheimer's, the work done with scans claims to measure these alterations. By analysing patterns of brain anatomy across populations, certain typical patterns or asymmetries in particular regions become visible. This line of research also builds on knowledge about variability—patterns of change typical of Alzheimer's can be ascertained beyond the normal variability to be expected.

Data about differences reviewed in the last section are further embedded in the atlas in the shape of probabilistic maps. Such maps indicate the normal distribution in space of particular features of the brain. They can also be oriented to pathology, and be designed to show the anatomical and physiological patterns typical of a particular clinical subpopulation (Thompson, Mega, & Toga, 2002). Disease-specific atlases are made up of the brain scans of specific clinical populations, and built as tools to show the probability that a specific brain scan shows a pattern of variations typical of a particular disease.

The work on Alzheimer's of this group located at UCLA draws on the observation that diffuse cortical atrophy is typical of Alzheimer's disease, among other dementias (Schmidt, 1992). Atlases are used to further characterise and quantify the atrophy specific to Alzheimer's disease. Like in the normal average brain, patients are matched for age, gender, handedness, and educational level. Using an MRI scan, a representation of the surface of the cerebral cortex is made, i.e. the hills and valleys of the surface of the cortex of a given subject are mapped. It is compared to an atlas of scans deemed to be normal. Areas in the individual's scan which vary from the norm (beyond normal variation) are marked on a brain map with 'hot colours'. It is then possible to compare a subject's anatomy with that of a

[25] W. van Tillburg, Summary and Conclusions, in E. C. Wolters, & P. Scheltens (Eds.), *Alzheimer's disease: Back to the future*, VU Amsterdam, 1993; quoted in Prins (1998) p. 193.

large population, and to determine whether variations are within a normal range (Thompson, Mega, & Toga, 2002). These comparisons are made using probabilistic approaches and very complex algorithms. It is also possible to match patients for specific clinical profiles (for example, levels of memory loss), and to make a series of atlases that might represent disease progression (Thompson, Mega, & Toga, 2002). These atlases also have multiple functions, as data and model. Like the atlases developed to investigate variability of the normal brain, disease-specific atlases can act as a quantitative framework that correlates various levels of study of the disease (structural, metabolic, molecular and histological) (Mega et al., 1997).

11. From object to norm

Just as the presence of plaques and tangles played a role in the struggle between psychiatrist and biomedical approaches in the treatment of senility and Alzheimer's (Prins, 1998), so the possibility of scanning shifts the diagnosis for Alzheimer's from neuropathologists to neurologically oriented psychiatrists and neurologists with access to a scanner and—not to be underestimated—the support of bioinformaticians. These brain databases, originally developed as research tools, have therefore been built up into data sets that have a normative potential. They can be used to indicate normal variation and pathological deviation. They are even being developed to trace individuals 'at risk', in more recent articulations, thereby placing this tool within the holy triad of bio-medical categories of normality, pathology and risk. It is further being extended to research in therapies for these conditions. This quantitative approach to measuring volumes or changes in shapes in relation to Alzheimer's has been pursued in humans and animals, with the added goal of providing biological markers for clinical trials (Redwine et al., 2003; Thompson et al., 2003). This line of work joins other highly informational ones in pharmacological and molecular biology research, where advanced modeling is used to explore new compounds, and where data-mining of databases is deployed.

These two examples of the experimental systems that have been developed around brain scans illustrate how the adoption of a framework for the analysis of digital scans shapes experimental possibilities. The experimental system around the virtual brain as an epistemic object is also shaped by the notion that the starting point for exploring the brain is a coordinate system, and that this coordinate system is implemented in a digital computerised system. Sophisticated manipulation of data in this coordinate system, and the application of complex algorithms, yield results about quantitative differences in anatomy and physiology between brains. Experiments focus on finding within this data set differences that are meaningful, consistent, or that can be correlated to other types of scans or to other information known about the persons whose scans are being analysed. These also yield new baselines and novel standards to further investigate the brain. Furthermore, the digital context of this work is used to sustain interactions between different disciplinary approaches and techniques. The informational version of the brain invites translations and connections. Of course, this flavour only becomes distinct in retrospect, as the virtual brain has stabilised as a distinct epistemic object, within an experimental system that has gained momentum.[26] The successful development of a research stream, and its consolidation as a new subdiscipline of neuroscience (cognitive neuroscience) also play an important role in making this epistemic object viable and recognizable.[27]

Even in the study of the normal brain, the use of digitalised maps of the mind requires the adoption of different standards of evidence. Here too there are trade-offs between the biologisation of the mental, praised as a grounding of cognitive science in the materiality of the brain, and the constraints of working in a digitised setting, within the limitations of scanning technology and experimental strategies. How a digitised and biologised approach to the mind and brain becomes an accepted scientific practice is a complex process of hybridisation and exchange between the cultures of neuroanatomy, psychology, and other neuroscientific disciplines.

12. Conclusion

Various aspects of the virtual brain have been examined here, and contrasted to other 'versions' of the brain. Brain databases were shown to have multiple roles. On the one hand, the database fulfils a similar role to the paper atlas, and builds on the tradition of pathological paper atlases. In that sense, they are not comparable to brain banks, which contain research materials. On the other hand, by making these collections of scans manipulable in a digital context, the atlas functions as a database, and therefore also as a source of research material—a function also fulfilled by brain banks. As an object of research, the virtual brain is both object and representation, both epistemic object and data, raw material and model. Comparisons of the collection, investigation, and circulation of wet and virtual brains highlighted that the virtual brain is an eminently malleable object, which has a different character than the solid and biologically foundational wet brain of brain banks.

Brain scans constitute an embarrassment of riches, tractable through the development of algorithms for processing, the automation of analysis, and the building of pipelines to transform raw scans into properly formatted, labelled, normalised, and analysable data. These manipulations, possible because of the digital format of scans, makes these atlases into powerful resources for neuroanatomy. Scans become frameworks and data can be 'worked up' to become a model. The atlas of digitized scans can therefore be a way of organising empirical data (collections of scans), a way of analyzing them, the basis for modeling of disease or of develop-

[26] See Rheinberger (1997) for a further discussion of the issues of hindsight and of whiggish history.
[27] This stability is always partial however, and the result of temporary arrangements. Attempts to have scans circulate outside their context of production, via data sharing databases such as the fMRIDC at Dartmouth College, US, for example, have met with scepticism from researchers.

ment, and also a way of detecting pathology. The informational infrastructure developed around these scans extends and multiplies them as objects of investigation.

The ties to various clinical concerns, and to the sciences of the mind, are also different for each type of brain. For the virtual brain, this relation is presented as a seamless chain, from investigation to detection to screening, sustained by the technology of the scanner, and its promise of 'application' of neuroinformatics findings. The map and network metaphors of the virtual brain emphasise both the tractability and complexity of the brain, and the possibility of coming to terms with these via the wonders of hypersophisticated computer technologies.

This comparison has therefore highlighted the new configuration of brains and technology with which this article began. This configuration, brought about by an informational turn, is sustained by two dynamics: the creation of digital object and the networked character of research. These changes amount to much more than the presence of new information and communication technologies. Indeed, there are interactions between the two types of brain collections. For example, post-mortem brains are also being included in one of the main digital atlases,[28] and scans have also been used to guide the preparation of brain tissue for brain banks (De Groot et al., 2001). There is also some work on the correlation of histological techniques that examine cells in brain specimens, with metabolic brain scans (Mega et al., 1997). The translations from tissue to scan or from scan to tissue, however, remain oriented to the primary object of each field. Brain slices are transformed into digital brain atlases, while scans are used to correlate what can be seen in a microscope.[29] The virtual brain is not merely supported by technology, but constituted by it. Research practices around this virtual brain in turn focus on an object of study that is an aggregate of digital data, and which is best manipulated using networked technologies. The experiments that are performed take on a data-driven character, and resemble more closely a process of exploration and discovery, rather than hypothesis-testing. I want to reflect briefly on the ways this characterisation of knowledge production differs from its predecessors.

[28] Tissues are frozen and each slice photographed and rendered digitally in one component of the work of the International Consortium for Brain Mapping (ICBM). They are then placed in a standard space, in order to be correlated with the other information in the atlas.

[29] In terms of more general presence of ICT, there also seems to be a growing use of databases to help with the documentation that is so essential to the quality and value of brain collections. The internet is also increasingly seen as an important medium to communicate with the constituencies (patient groups, researchers) who might contribute or make use of the brain bank. Brain banks use their sites as ways of distributing information packages to potential donors, or to register donors. The Brain Bank workshop of 2002 noted in its recommendations that 'use of PM [post mortem] tissue for structural and functional studies of the brain meshes very well with neuroimaging results', and that the various brain banks should be networked via a common database. Proceedings of a Mini-symposium: Substance Abuse and Neuropsychiatric Disorders at the International Workshop on Brain Banks. March 11–12, 2002 (http://www.nida.nih.gov/whatsnew/meetings/BrainBank/Recommendations). Both types of collections are being linked to databases in the areas of proteomics and genetics.

An interesting epistemological issue that arises is the 'penetration' of technology into the constitution of objects. In philosophical terms, the fact that these objects are so dependent on technology is not so different from arguments about the theory-ladenness of observations in scientific practice (Hacking, 1983). The informational turn is probably more interesting in sociological terms, regarding the kinds of settings in which scientific work can be pursued, and the various dynamics that shape and make technologies available for scientists. Focusing on this level also has the advantage of making tangible the materiality of a practice that is often cloaked in the garb of transparency and invisibility (Haraway, 1991; Hayles, 1992). In the case of the virtual brain, this involves investigating the tension between the claims to non-invasiveness of scanning, and the subsequent presentation of bodies as thoroughly informational objects. The paradox of bodies that are not touched, yet captured in molecular detail, may be the commonplace of an informational world.

Second, I have highlighted the circulation and transformation of scans into various kinds of aggregate objects. This malleability is different in important ways from the 'immutable mobile' associated with the printing press (Eisenstein, 1979; Latour, 1990). With the immutable mobile—the basic unit of knowledge-making for the modern state—stability and compilation of objects are warranted by aggregation and summary. In a digitised informational setting such as that of the brain atlas, transformations of data are algorithmic and probabilistic. This means that the tension between the single case and the class of phenomena studied can be maintained, in a way that is impossible without significant computational power.[30] The promises of digitality emphasise the possibility of shifting the object across multiple layers of analysis, while retaining its integrity as unique. In this and other cases dealing with bodies or individuals, objects remain unique in the sense of being tied to unique individual selves. This particular possibility of inscribing one individual self within a scientific representation is not only something that is impossible with post-mortem studies, but may also indicate a special form of the phenomenon of biosociality articulated by the anthropologist Paul Rabinow in relation to genetic technologies (Rabinow, 1992).

The manipulations and transformations of data in working with the virtual brain are related to chains of inscriptions (Latour & Woolgar, 1986) and to the importance of textuality for the circulation of traces. Indeed, as the historian of science Hans-Joerg Rheinberger, reflecting on the importance of the chain of differential marks, wrote: 'the enterprise dubbed "modern science" derives its power from its peculiar spaces of representation' (Rheinberger, 1997). Differences in the space of representation of informational science are therefore likely to have significant consequences for what we think of as science and knowledge. The issue, addressed

[30] Bowker and Star note the increased possibility for maintaining, for longer in the analytic process, sets of multiple factors in analyses, a possibility that would not be feasible without computers, since paper and pencil manipulations require closure and reduction. For a description of a similar dynamic related to the transformations of brains to atlases, see Beaulieu (2002), p. 21.

here in terms of brains, is: to what extent do technologies of inscription and manipulation of traces differ in digital settings?[31] To restate but one example of the consequences of these differences, the blurring of distinctions between data and experiment in brain atlases makes it difficult to retrieve the categories of object and experimental system.

Another important transformation of representational practices is the increased reliance on visualisation. Visualisation is often praised as a powerful interface between humans and data. This interface is functional in the lab, it is argued, since it allows interaction between researchers and large amounts of data that would otherwise be intractable. The visual as interface is also present in encounters between lay people and scientists who display their work. These types of visualisations rely on high end computing and networked computing technologies, and are a relatively new dimension in all but a few fields such as atmospheric science, astronomy and physics (and of course, 'defence' research). The fields discussed here—neuropathology, neurology and neuropsychology have traditionally been rather 'low-tech'. The growing presence of this mode of representation is therefore likely to make even more prominent the need for 'visual knowing' (Stafford, 1996).

Besides these features of digitality, which remain to be further theorised and explored, the notion of network is an important motif in the emerging neuroscientific views of the mind and in the organisation of research. Networks in the brain are a way of reading functions, effects of genes, and effects of environment, so that investigating the brain and its networks produces a totalising account of the self. Indeed, it seems that the metaphor folds back onto itself, when neural network technologies are used to explore multi-dimensional data about the brain:

> The growth of brain imaging databases also presents opportunities to determine unforeseen patterns in large datasets with exploratory data mining or data profiling techniques ... These techniques use information theory ... and neural networks to uncover fundamental factors that govern variation in datasets. (Thompson, Mega, & Toga, 2002)

More generally, the network may also be the dominant feature of informational science, where networks of collections, databases, and data warehouses form a virtual, distributed workbench. Along with a growth of the size of digital data sets, there is therefore an increased interest in tools and skills for handling this growing amount of information. These include new methods for regulating the acquisition of data, and sophisticated skills in the manipulation and analysis of information. As such, a focus on informational practices and infrastructure around networks should be fruitful.

Finally, a new politics of informational knowledge may also be developing. Surveillance, control, and management have been identified as the political and cultural manifestations of information and communication technologies in knowledge

[31] Lynch's analysis of opticality and digitality contains further useful indications of how these representational systems might differ, Lynch (1991).

production (Robins & Webster, 1999). With the types of objects and resources described in this article, these issues can be detected, for example, in the potential applications of these techniques for screening. Other political issues also arise, however, that are more specifically related to the networked character of informational science. Questions of 'access' to these resources, and concerns with the increased circulation of potentially sensitive data are two important examples of such issues. These are also aspects of a developing configuration of technology and research practices, which reshape expectations about both how we can know and what we can know.

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