Mobilising experimental life:
Spaces of becoming with mutant mice

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Abstract

This paper uses the figure of the inbred laboratory mouse to reflect upon the management and mobilisation of biological difference in the contemporary biosciences. Working through the concept of shifting experimental systems, the paper seeks to connect practices concerned with standardisation and control in contemporary research practices with the emergent and stochastic qualities of biological life. Specifically, it reviews the importance of historical narratives of standardisation in experimental systems based around model organisms, before identifying a tension in contemporary accounts of the reproduction and differentiation of inbred mouse strains within them. Firstly, narratives of new strain development, foregrounding personal biography and chance discovery, attest to the contingency and situatedness of apparently universal biotechnological production. Secondly, discoveries of unexpected animal litters challenge efforts to standardise mouse phenotypes and control the reproduction of murine strains over space. The co-existence of these two narratives draws attention to the importance of and interplay between both chance and control, determination and emergence, and the making and moving of experimental life in biomedical research. The reception or denial of such biological excess reflects the distribution of agencies and the emerging spatialities of the global infrastructures of biotechnological development, with implications for future relations between animal lives and human becomings in experimental practices.

Keywords

Mutation, emergence, becoming, standardisation, spatiality, model organisms, experimental systems

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'Trust no-one; repeat everything' (Anon[1])

'Repetition belongs to humour and irony; it is by nature transgression and exception, always revealing a singularity' (Deleuze, 2004: 6)

Introduction

I want to begin this paper by posing the question: what might it mean to become with an inbred mouse? This could seem an inauspicious starting point. The possibilities for 'becoming with' other species tend to focus on more charismatic animals than mice. The mouse is more often found in liminal spaces: relegated to children's literature, abjected as pest or marginalised as laboratory artefact. Nevertheless, these nonhuman animals are increasingly central to biomedical understandings of human corporeality, as the material and discursive practices of science draw new relations between the bodies of in-bred mice and the clinical symptoms of human disease. In this paper, I focus on the making of these animals and the mobilisation of their biological similarities and differences, to humans and each other, within the changing experimental systems of contemporary biomedical research[2]. These everyday accounts of managing mutation in mouse models of human

[1] According to one informant, interviewed in 2010 as part of the research which underpins this paper, this mantra was repeated to all new mouse researchers in the genetics laboratory of a well-known university in the USA.

[2] This paper draws on research completed as part of a set of projects around 'Biogeography and Transgenic Life', funded by an ESRC research fellowship, grant number RES-063-27-0093. It is based on ethnographic research and in-depth interviews exploring the changing production, circulation and regulation of genetically-altered mouse models in biomedical research, in Europe, the USA and Singapore from 2007-2010. The research involved around 90 interviews with a diversity of research scientists, laboratory veterinarians, animal welfare scientists and charities, funders and regulators, as well as participation in research meetings, site visits, online discussion lists and international conferences. All participants and locations in the ethnographic research were fully informed about the aims of the research and offered anonymity. This research was supplemented by review of the published literature in scientific journals and via publicly available websites. Names of individuals and places are used, when relevant, for the material drawn from these sources only.

disease are relational, revealing the essential, but inherently asymmetrical, relationalities of interspecies becomings in biomedical research. These narratives have spatial implications, indicating how global biomedical research valorises both standardisation and emergence in different geographical and experimental settings. They also have theoretical significance in the search for openness and creativity in ethics, art and human life via biological emergence (see for example Bennett, 2010; Grosz, 2008). Such social theoretical accounts represent an important shift in the way the materiality of life is understood and narrated as aleatory, excessive and differentiating, rather than construed as narrowly determined, conveying the 'dread of sameness' which accompanied cultural anxieties around genetic replication (Bishop, 2011; see also Jasanoff, 2006). This is a welcome shift, yet it is one I want to set in conversation with accounts from biomedical researchers working with mutant mice, to explore more about the patterning of this biological potential, and its negation, in contemporary research practices. This paper is thus an intervention into narratives of the development of model organisms, within the experimental systems of biological research Rheinberger (1997)[3], which is alert not only to the spaces of standardisation and repetition, but also to the cartographies of struggling with difference.

There are several contemporary contexts important for considering this relay between social theory, narratives of becoming and the spatialities of biomedical research. First, is the increase in use of mice as model organisms for understanding human biology and disease (Abbott, 2004; see also Austin et al, 2004; Balling et al, 2000; Grimm, 2006). Following a period of international collaborative research focused on gene mapping (Gaudillière and Rheinberger, 2004), biologists are increasingly returning to work with model organisms to make biological and clinical sense of genomic resources. A wide range of so-called post genomic approaches are remaking the questions it is possible to ask about biological entities, relations, processes and potentialities (Davies, 2011; Franklin, 2006; Sunder Rajan and Leonelli, forthcoming). Laboratory mice are central to many of these efforts, especially in the experimental systems of functional genomics, which aim to connect genomic

[3] The concept of an 'experimental system' is taken from the work of historian of science Hans-Jorg Rheinberger (1997). As an actor's category, this reflects the way scientists understand the structure and part of the modern empirical sciences on which they work. As Rheinberger (1997: 19) explains 'the notion of experimental systems is frequently used by scientists in biomedicine, biochemistry, biology and molecular biology to characterise the space and scope of their research activity. Whoever asks a contemporary laboratory bioscientist what he or she is doing will be told about his or her "system" and the things that happen there.' Rheinberger elaborates on this concept, emphasising its materiality and complex temporalities, to explore the ambiguities inherent in the differential reproduction of experimental systems. I pick up these more analytical points, and the oscillation between technical objects and epistemic things, in the following section.

knowledges to understandings of biological functions at the level of the organism. The questions about becoming with mutant mice are thus deeply relational; but they are also asymmetrical. Our understandings of human corporeality and potentiality are increasingly enacted through the individual bodies and multiple forms of a multitude of laboratory mice (Davies, 2012; see also Birke, 2003; Burt, 2006; Haraway, 1997). These both undercut human exceptionalism and reinscribe the role of human agencies in the lived lives of animals and humans. It is a complex, never innocent, and for some troubling, form of what Haraway (2008) would call 'becoming with'[4], in which the power to define the experimental lives of and knots of relations between animals and humans is at stake.

The question of what might it mean to become with an inbred mouse is not only about relationalities, it is also about spatialities, whose contours are changing with the increasingly international scope of biomedical research[5]. There is a complex spatiality enacted as the process of 'becoming with' such laboratory animals is at the same time a practice of 'becoming worldly' (Haraway, 2008). Inbred mice, and their genetically altered descendents[6], have achieved a particular universality and depth of entanglement in biomedical research practices through their insertion into international scientific networks as 'an ordinary commodity in the exchange circuits of transnational capital [...] a scientific instrument for sale like many other laboratory devices' (Haraway, 1997: 79; see also Michael, 2001). This is a particular way of becoming worldly, as experimental organisms developed in one laboratory become standardized technical commodities, spreading from

[4] The term 'becoming with' is taken from the work of Haraway (2003, 2008, 2010). The term emerges most fully in her consideration of companion species, which encompasses not only familiar companion species, such as dogs, but also more unfamiliar living things, such as bacteria, fungi and protists. Mice feature in her earlier work (Haraway 1997). The concept and processes of 'becoming with' demand consideration of the webs of relations, inter and intra-actions between species. This relationality is intricately placed, in the situated histories and geographies of actual living beings, differentiating it from the more abstract 'becoming' of Deleuze and Guattari (1987). Thus, for Haraway, the term is more than a metaphor and draws inspiration from Margulis's work on 'symbiogenesis'; though the potential for becoming with can be limited or curtailed by industrial and other processes.

[5] As historical geographer David Livingstone suggests, 'Space is rapidly becoming a central organizing principle for making sense of scientific knowledge' (Livingstone, 2010: 3). To talk about the spatialities of science is to attend to the properties by which scientific practices relate to and occupy space. This includes consideration of the social, material, institutional and technological characteristics of those places which are privileged 'truth-spots' (Gieryn, 2002) for the production of scientific knowledge, as well as the heterogeneous assemblages through which scientific knowledges travel over space (Secord, 2004). These spatialities are not given simply by geography, they are multiple, relational and always entangled with the different ways of understanding biological entities themselves (see for example, Franklin 2005, 2006). The spatial relations essential to the legal constitution and use of laboratory animals is the specific focus of work by Asdal (2008).

individual research centres, through specialised laboratory suppliers, to become the patented property of international biotechnology. Thus, mice are part of the story through which biology becomes molecular, genetic life commodified and genetic explanations fetishized (Robins, 2008; Lezaun, 2007). Yet, here as well Haraway's question 'How is becoming with a practice of becoming worldly?' (2008: 35) is opened up in the context of the post genomic sciences. Post genomics is not simply interested in the reproduction of standardised laboratory animals, but is also concerned with the production of biological difference through genetic modification, enabling exploration of the complex processes linking animal genomes and different phenotypes. Epigenetics is part of this enquiry, but so is geography too, for phenotypes have environmental, as well as genetic, components (Spector, 2012). This increasing attentiveness to variation means the making and moving of experimental life requires places and procedures which work towards the centralisation of biological standards and articulate practices which are sensitive to difference (see for example Leonelli, 2012).

'Becoming with' mutant mice thus has different dimensions, for international biomedical researchers collaborating in new ways and spaces using mice as model organisms, and for others too. For scientists and technicians, mutant mice are increasingly essential companions on the route to becoming an experimentalist, epistemologist, or animal caretaker. For the wider population of patients-in-waiting, these animals are now thoroughly enmeshed in the assemblages of scientific apparatus, diagnostic tests, and therapeutic drugs we use to treat the range of our (post)human disorders. For the animals themselves, the different answers to what it might mean to become with an inbred mouse in different spaces have vital consequences for their species identity and individual experiences. Mutant mice have become an increasingly common 'companion species' in laboratories developing new biomedical understandings and therapeutic interventions, even if we would eschew this term. The long history of the use of animals in reconstituting ourselves as technoscientific subjects means we have to take their changing reproductive forms seriously. As Haraway puts it, 'literate in the reading and writing practices proper to the technical-mythic territories of the laboratory, we have little choice. We inhabit these narratives, and they inhabit us. The figures and the stories of these places haunt us, literally' (Haraway, 1997: 172).

[6] I use the terms genetically-altered or mutant mice in this paper to refer to all laboratory mice whose genomes have been altered through breeding techniques or genetic modification to shape them for the

To talk of becomings and hauntings is thus to look in two different directions at the same time. There is a complex temporality involved in thinking what it might mean to become, now, with a genetically altered mouse. Look backwards, and there are histories of the standardisation of biological forms, the practical associations between mice-breeding pioneers and production-line technologies, and the displacement of the individual mouse body to the genetic identity of the inbred strain, as DNA becomes the master molecular of molecular biology (Rader, 2004). In this history, there are ways of narrating the development of mice as model organisms, which paraphrasing early Latour (1987), would talk of the inscription and standardisation of biological properties around centres of calculation, immutable mobiles and continuous control. Yet, look forward, and the possibilities of post genomics appear more open, with the potential to engage these animal's biological mutability. Here the contextual and relational choreographies of Haraway's 'becoming with' meets other theoretical and philosophical inflections, of Deleuze's writing on 'becoming animal' or Derrida's notion of Différance. Perhaps there are ways of telling stories about the proliferation of laboratory mice, which recapitulating Deleuze and Guattari (1997), would talk of becomings, swarms of animality and difference, and might find in the openness to new relations heralded by the proliferation of post genomic approaches a 'form of repetition which is always fully positive and affirmative' (Bearn, 2000: 441)[7].

In this paper, I want to keep these dual theoretical registers in play, but look more closely at the spaces and ways in which scientists and animal caretakers talk about the mice with which they work. I narrate two different kinds of stories that circulate from the mouse house: the stories told about the discovery of new mutant strains and the detection of unexpected, litters or 'virgin births'. These narratives reveal how new relations between animal biology and human disease take shape and are inserted into context. These relations are not fixed, but performed, in part through the narratives that are told about them. Narratives in science, as elsewhere, are important as they order histories as well as pointing towards futures: framing temporality, allocating cause and effect. Taking stories seriously helps identify how agencies are attributed and methodologies accepted by respondents themselves (Traweek 1992; see also Davies, 2000). They are also often intricately located, drawing attention to the importance of key sites, whilst acting as discursive devices through which action is (literally) more widely articulated. Narratives are an important part of how science travels, through shaping expectations, sharing norms and establishing practices.

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purposes of experimental research. The more specific term, inbred strains, is defined later in the paper.

[7] See also footnote 4.

I introduce first the more conventional narratives of the standardisation of laboratory animals, exploring their genetic and spatial implications, and drawing attention to their temporalities in dialogue with Rheinberger's (1997) work on experimental systems. I then explore tensions between two forms of narrating the management of genetically altered mouse strains in contemporary research. Stories of unexpected events in the mouse house illustrate how animal caretakers and scientists seek to makes sense of spontaneous mutations in laboratory mice. These moments of differential biological reproduction either herald a useful new strain of research animal, or the animals are killed; they either provide an occasion for openness to biological becoming or are culled in the search for genetic control. I am interested in when and where these different outcomes occur. There are, I suggest, vital differences between the two, whose contours can be traced to understand what influences these different forms of 'becoming with' and the changing cartographies of 'becoming worldly'. From Haraway, I suggest these encounters have implications for the making of technoscientific subjects, which mix animal mutability and the potential for human therapeutics. From Rheinberger, I contend these moments of emergence help understand the spaces through which these animal's becomings might 'let things happen in a different way in the future' (Rheinberger, 2007: 2). Concluding, I suggest these becomings are ultimately recognised in relation to human ends, and moreover, despite the growing internationalisation of science, there are a limited number of sites through which mutant mice can move between being a standardised technical object and a new epistemic thing.

Standardisation and the making of mice

Most histories of the production of laboratory animals in the twentieth century tell stories about the quest for homogeneity in the pursuit of reliable supplies of animals and the achievement of replicable research. The subtitle of Karen Rader's history of *'Making Mice: The Standardizing Animals for American Biomedical Research, 1900-1955'* emphasises this practice in North American biology, but this is also the dominant narrative in Europe, in the work of Löwy and Gaudillière (1998), Birke (2003) and Kirk (2008). Rader's account of the development of mouse genetics and the provision of standardised laboratory animals focuses on the history of the Jackson Laboratory, Maine USA, which was founded in 1929 by Clarence Cook Little. Historically, the Jackson Laboratory has been a leading institution in the development and distribution of laboratory mice for genetic research. It is not the only

site. A comprehensive history of the development of mouse genetics would include the large laboratories at Cold Spring Harbor (USA) and Harwell (UK) in the UK, the later capacity and innovation provided by national government and commercial laboratory animal suppliers, and a range of smaller research institutes. But, especially for inbred mouse strains, it is an internationally important site, in the past and today. The Jackson Laboratory remains both a genetics research institute and one of the world's leading repositories for mutant mouse variants. It now supplies a huge range of genetically altered mice to the international research community, including spontaneous and induced mutants produced through a range of genetic technologies. However, its reputation was built around the production and maintenance of inbred mice strains, and it continues to define the 'gold-standard' type for many inbred strains still used today[8].

Inbred mice strains are populations of animals that are isogenic. The individual animals of an inbred strain have been standardized at the locus of the gene by repeated brother-sister matings; something it is possible to achieve with mice, but not all animals. The founder animals for each strain are selected according to the identification and breeding of desired biological traits relevant to a specific programme of scientific research. In the case of Little, a Harvard trained geneticist, working in the 1920s and interested in mammalian genetics and cancer, this was a spontaneous but hereditary tendency that some mice had to develop mammary cancer. As Rader (2004) explains Little initially sourced mice with interesting characteristics from a range of hobbyist breeders, scaling these practices up to provide a consistent supply of identical animals for scientists working in universities, medical schools and research institutes. Funding for the Jackson Laboratories was facilitated by Roscoe B Jackson, then president of the Hudson Motor Car Company, who noted the 'value of standardized strains for making biomedical research more like a Detroit factory assembly line [… adding …] efficiency, accuracy, and repeatability to biological work' (Rader, 2001). Securing the interest of researchers in these standardized animals required policy shifts in US federal funding for cancer research, continued economic investment to scale-up the production of inbred lines, as well as public campaigns to cast mice as the unlikely heroes in an emerging war on cancer (Rader, 2004). Little campaigned repeatedly on the centrality of genetics to the future of cancer biology, arguing previous experimental data had 'many statistical artefacts due to the mixed genetic nature of the mice used' (Rader, 2001), downplaying other environmental causes of cancer, including smoking.

[8] For the Jackson Laboratory promise on 'Gold Standard' mice see URL http://jaxmice.jax.org/jaxnotes/504/504c.html and http://jaxmice.jax.org/findmice/why.html (last consulted

The meaning of standardisation in this case is thus two-fold, with epistemic and spatial implications. First, there is the standardisation of the animals around specific gene loci to develop replicable animal models of human diseases. The inbred mouse strain is managed to reproduce itself in terms of its genotype, reducing 'noise' from genetic fluctuations and other environmental effects. It is through the consistent repetition of the animal's genotype that the unruly biological complexity of the animal can be temporarily forgotten, as a positive accomplishment (Deleuze, 2004: 9), enabling its insertion into the experimental systems of mammalian cancer genetics and then molecular biology. Standardisation around a particular concept of the gene enables the mouse body in a single experiment not only to speak for all other mouse bodies, but, through genetic homologies, for the human body too. As Rheinberger (1997; see also Canguilhem, 2000) suggests, the experimental systems of molecular biology embody a particular epistemology of life, premised on the positioning of 'code' or 'information' as the basic biological unit. The emerging emphasis on gene as information from the 1950s, articulated effectively with the management of inbred strains to reduce the statistical experimental artefacts caused by genetic variance. The inbred mouse strain, standardized at the locus of the gene, thus becomes a 'neat genetic tool'[9], widely used, not only in cancer research, but also throughout the 1990s as proof of concept within molecular biology. This shared understanding of life, framed in terms of genetic information and communication, underpinned the successful operation of the Jackson Laboratory as both a centre for cancer research and a supplier of inbred strains to other research laboratories nationally and internationally.

A second set of standardisation processes are thus required to enable inbred mice to function as standard model organisms, across different disciplines and different geographical contexts. Standardisation is thus simultaneously a spatial process. Indeed, the link between movement and repetition is woven into Deleuze's questioning of 'what it means to "to produce movement", to repeat or obtain repetition' (Deleuze, 2004: 12). The scaling up from the locus of the gene to achieve a standardized animal body for each experimental instantiation requires the creation of further standards, for cage size and design, for husbandry procedures and operating protocols, so that the whole experimental systems can be replicated in different laboratory spaces. This is embodied in the now

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September 2011)

[9] This term was used by several respondents to whom I spoke to in my research. It both characterises the importance of inbred mouse strains to the development of genetics, but also indicates the challenges of using these animals in post genomic research.

standardized architecture of the mouse cage, the stacked individually-ventilated cages, and built structures that house large mouse vivariums in international sites for biomedical research. However, breeding inbred strains in isolation generates differences between populations, through environmental effects, genetic drift, and chance mutations[10]. The large animal colonies inhabiting these mouse houses thus require the careful management of their reproductive capacities towards replication and away from mutation. Animal caretakers and technicians organise appropriate matings, and remove unwanted deviations, ensuring the constant supply of identical animals at different sites. Some processes, notably spontaneous mutation, cannot be controlled, so the animals have to be periodically restocked from the parent population kept by the central supplier, ensuring their continued equivalence to the rest of the named inbred strain[11]. It is the dual processes of genetic and spatial standardisation that have secured the continued centrality of Jackson Laboratories as the main international provider of inbred mouse strains, and of the inbred mouse's ability to function effectively as what Rheinberger would call a 'technical object' in contemporary biological research.

Rheinberger's (1997) work on the development of molecular biology provides a way of holding onto the complex orderings and becomings at play in experimental systems, especially in terms of the oscillation between technical objects and epistemic things. Rheinberger identifies a dynamic in science between *epistemic things,* which are the objects of enquiry in a given experiment; and *technical objects*, which embed and articulate the experiment with what is already known. Epistemic things are necessarily underdetermined. This is inevitable; they embody what one does not already know and allow experimental practices to generate novelty. Technical objects, in contrast, are the instruments, inscription devices and model organisms, with given standards of purity and precision, which allow researchers to make sense of the unpredictable behaviour of epistemic things. That experimental systems comprise both known technical objects and underdetermined epistemic things allows them to replicate themselves, whilst also remaining arrangements in which new kinds of knowledge can be generated. He acknowledges there is a blurred line between the two, and this negotiation is central to innovation in science.

[10] For further research on the handling of species character and genetic difference in transgenic animals through ethics protocols and research practices see Holmberg (2010) and Holmberg and Ideland (2009).
[11] Usually twenty sibling matings are required for a genetic trait to be stabilized within a breeding population to achieve an inbred strain. Thus, if a well characterised inbred mice population is distributed to two different locations and the two populations allowed to bred separately, it only takes ten generations for the mice to be considered to belong to two different substrains.

Rheinberger develops these concepts through historical research on the test-tube synthesis of proteins in the 1950s, which preceded the discovery of DNA. In this period, and in Rheinberger's case study, animals are increasingly relegated to the role of technical objects as they become standardised and incorporated into the artefacts and architectures of the laboratory. In his account, 'laboratory rats' are placed alongside the amino acids, centrifuges, and so forth which support but are not the central to the experimental systems of molecular biology. Look up rats in the index of his book and you are cross-referenced to rat liver incorporation system. Mice do not figure at all. This is a concept derived from the study of a scientific community and experimental system focused around the synthetic production of proteins and the identification of RNA. That research animals, and their derivatives, are figured as technical objects in this account is in accordance with the particular communicative paradigms of early molecular biology. Expectation of the fundamental and central metaphor of information in explaining biological characteristics relegates the animal body and the biology of the whole organism to a subsidiary position.

Yet, mice have not been incorporated into the practices of biomedical research in just one way. Even in the early years of the Jackson Laboratories there were distinct strands of work, focusing on cancer research and transplantation studies, as well as sections of the facility concentrating on breeding mice for supply and sale. At other sites, such as Harwell UK, mouse genetics has a different history, in the testing of nuclear radiation on animals, using large mouse colonies to quantify the mutagenic effects of radiation, and at times identifying new mutant strains of value to other scientific researchers[12]. The precursor to the journal *Mammalian Genetics*, *The Mouse Newsletter*, was set up in the 1950s as an informal publication to connect mouse researchers and collect information on new mouse strains internationally. The complex genealogies of inbred mice (Beck et al, 2000) is reflective of this long history, but also geography, demonstrating the development of unique strains of mice in geographically distinct endeavours in Europe, the USA, China, Japan, and elsewhere. More recently, large-scale collaborative and community projects have begun to create and collate a range of mutant mice using genetic techniques, such conditional knock-outs and ENU mutagenesis, to create additional genetic alterations on inbred and other strains (Balling et al, 2000). These are organised around different techniques in functional genomics, and in many cases are seeking to reconnect research in different geographic

[12] This process of large-scale mutagenesis has a parallel with the process of developing drosophila mutants for genetics, as characterised in Kohler (1994).

locations. They already face the challenge that an inbred strain used in one location is not necessarily the same as that in another.

Laboratory mice are thus at the centre of more than one experimental system and in more than one place. Furthermore, these inbred animals are not simply incorporated into scientific research as standardized technical objects; they can, at times, be epistemic things as well. This role is reopening as contemporary events in the post genomic sciences shift understandings of the epistemologies, temporalities, and spatialities of life once again. As a number of commentators have observed, 'we are not witnessing a linear progression towards a general molecularization of life, but rather, and more interestingly, inflections of a rebiologization of life' (Rabinow and Caduff, 2006; see also Franklin, 2006). The challenge of making biological sense of the huge amount of genomic information generated through molecular technologies is reworking experimental understandings of what kind of an object or thing a genetically altered mouse might be. They continue to play key roles as technical objects in many experimental procedures; they are also emerging as the favoured epistemic things in research on functional genomics. Here, novel understandings of gene interaction and function are sought through the production of a new round of mutant animals, whose unexpected and unknown phenotype is the aim of experiment, of potential value for increasing knowledge about what genes do (Davies, 2011). Insights from across the post genomic sciences have demonstrated that genetic communication is not independent from the noise – the 'junk' DNA and previously overlooked epigenetic effects – and there is an intensification of experimental inquiry on complex interactions and at multiple scales. As Franklin puts it, 'the silence of the genome has given way to the cacophony of the epigenetic' (2006: 169). In the context of post genomics, stories of standardisation are no longer adequate on their own; they run alongside the revalorisation of biological difference and unexpected emergence.

This renewed emphasis on animal becomings has implications for the roles played by researchers, technicians, patients and for the processes by which the singular event of an animal 'becoming otherwise' is linked to the wider processes of things 'becoming worldly'. Compared to the apparently context-free coding functions imagined of early genetics, post genomics turns out to have explicitly spatial components. Contexts matters to the different technical and epistemic questions laboratory animals are being asked to answer. Epistemic and technical roles exist alongside each other, raising questions about what influences the mouse's identity as technical object or epistemic thing in different times and spaces. Of

course, one answer to this is epistemology: what is the particular configuration of apparatus and animals assembled for the aims of each particular experiment? But, as in the past, the institutional, economic and spatial play a key role too, influencing the extent to which emergence is controlled and where understandings of life and relations are able to shift.

Emergence and the Moving of Mice

In what follows, I trace the interplay between animal identity as technical object and epistemic thing, not within the event of the experiment, but through the process of provisioning laboratory animals. The multiple and dispersed centres of mouse breeding, whether commercial (e.g. Harlan, Taconic, Charles River), non-profit (e.g. The Jackson Laboratory) or government-funded (universities and other research centres), are important but overlooked sites, where potentialities for both replication and mutation co-exist before their insertion into specific experimental systems. The work of animal technicians and caretakers in facilitating experiments with animals is explored by Birke et al (2007). Animal caretakers breed and care for animals, acting as mediators between the animals' needs and the demands of scientific research, and providing the affective skills that aid the reproducibility of animal experiments. They also play a key role in ensuring that animals with the appropriate genetic background or genetic alteration are supplied to researchers: in delivering either the normal or the pathological. Here, there are stories about deviants, mutants, virgins, and rogues. These are not my terms, but are used by research respondents to talk about the animals in their care. The terminology takes us back to the monstrous bodily overspills of early taxonomy; however, the context is twenty-first century biology. These terms emerge as animal caretakers and scientists seek to understand the challenge that spontaneous mutations in laboratory mice present to their work. Either unexpected happenings in the mouse house herald a useful new strain of research animal, or the animals are killed. Either the animal technician is able to make the leap from the supporting role of providing technical objects to potential researcher exploring things of epistemic interest, or they are not. In what follows, I explore where and when these different outcomes occur.

Mutant mice and the recognition of biological potential

Firstly, there are the stories of mutant mouse discovery. These accounts punctuate assumptions of universal qualities, which position inbred mice strains as place-less and temporally-stable technical objects. When recounting the identification of new mutant animals, clearly identifiable characteristics of place re-emerge, and new forms of difference between animals and potential equivalences with human biology are fore grounded. These moments of biological emergence are intricately located and personally narrated, revealing the ultimate singularity that underpins every existing mutant animal or other inbred strain. In the vocabulary of Holmberg and Ideland (2009), these are the 'ordinary treasures' of transgenic research, exemplifying the hopes for future medical treatments, whilst silencing other dilemmas about their use.

The following is one published in the Jax Notes newsletter, in 2006, when animal technicians and researchers reported the discovery of a new animal phenotype in the breeding facilities of the Jackson Laboratory.

> 'At the very moment when Jackson Laboratory biologist Peter Reifsnyder was in the doctor's office being diagnosed with sleep apnea, a sleep disorder that troubles roughly 12 million Americans, some animal technicians in one of the Laboratory's mouse rooms were curiously observing a very odd behavior by individuals of a mouse strain called New Zealand Obese (NZO/HlLtJ). The mice were standing vertically upright on their hind legs - while sleeping. When Reifsnyder himself observed this behavior, he immediately suspected that it was a kind of sleep apnea. The discovery of this unusual behavior in mice is a significant breakthrough because, until then, the only known animal model of sleep apnea was the English bulldog.'[13]

The report continues the narrative, suggesting this initial moment of discovery prompted the search for other mice in the facilities, which might exhibit different sleep behaviours.

> 'The discovery of the unusual sleep behavior of NZO mice prompted some Jackson Laboratory staff to examine other mouse strains for similar behavior. They soon discovered that two other strains of obese mice and two strains of lean mice exhibit fragmented sleep - though none of these strains were observed standing while sleeping'

[13] http://jaxmice.jax.org/jaxnotes/504/504f.html (last consulted August 2012)

It then concludes with some more speculative comments about the potential of this newly discovered animal behaviour for understanding the genetic component of and developing new treatments for human sleep disorders.

> 'Research indicates that the cause of sleep apnea is at least partly genetic. Identifying the alleles responsible for sleep disorders in mouse models could help researchers find the fundamental cause of and better treatments for sleep apnea.'

In this narrative, the mouse moves swiftly from being an apparently identical member of an established inbred strain, being reassembled via the work of the laboratory staff and the imaginative projections of the biologist, to become the focus for a new round of epistemic questions. This description is taken from the *Jackson Notes*[14] and its tone is journalistic. However, even within the main mouse database, there are similar stories of new strain development rendered in the more technical language of mouse nomenclature, but still attributing the same characteristics of biography and geography to the apparently universal inbred strain. This is one, selected from the thousands of mutant mice available from the Jackson laboratory, which is a mouse model for human skin disorders:

> 'This cpdm spontaneous mutation arose in a colony of C57BL/KaLawRij held at TNO-Institute in the Netherlands. Mice from the cpdm colony were sent to Dr. John Sundberg at The Jackson Laboratory in 1993, and were maintained by sibling matings in a private research colony until they were donated to The Jackson Laboratory Repository in 2007.'[15]

The language here is more specialized, but the structure of the narrative is the same. It emphasises the time, people and places in which interesting new animals emerge, and the route taken from the mouse house to the research laboratory, where they have the potential to become surrogates for studying human disease. The process of animal becoming a new model for human disease is linked to the process of becoming worldly through the hybrid role of Jackson Laboratories as both research centre and repository. The Jackson Laboratory remains a key location for mouse genetics: a centre, not necessarily of simple calculation, but for managing the processes of becoming.

[14] The JAX® NOTES was the quarterly print newsletter produced by the Jackson Laboratories 2012. It has now been replaced by a monthly JAX eNews.

Virgin births and the negation of biological emergence

In contrast to these stories of productive phenotypic traits are the narratives of virgin births. Again, this is not my terminology[16]. The term was used alongside the more neutral vocabulary of 'unexpected litters' in an exchange on the mouse genetics discussion list[17]. Here, animal caretakers exchanged stories about the presence of unexpected litters in the cages of their mouse breeding facilities. I had been following this list for a while and was intrigued by the contrast between these stories of virgin births and the narratives of mutant mouse discovery. I contacted the people with follow-up questions, told them about my research, and asked for their permissions and their stories. They came back with slightly different versions of this story, but the following captures the general tone:

> 'My experience with "virgin births" in my mouse colony occurred over a year ago, was limited in time to between 3 and 6 months, and has never happened before or since. We were surprised to find litters in breeder cages, which we thought we were not currently breeding. We attributed the first 1 or 2 cases to bookkeeping errors on our part, but as more occurred, I could not believe we were making that many mistakes and started to look for other possibilities.' (Animal technician, by email, 2008)

The explanations put forward for these unexpected litters were varied. In all cases, there had been no known mating, so until a candidate male was found they were talked about as virgin births. In some instances, unexpected litters emerged shortly after another litter was born and weaned. Postings to the list suggested inbreeding or spontaneous mutations might have resulted in strains that were sexually mature before weaning. As one animal caretaker wrote:

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[15] http://jaxmice.jax.org/strain/007599.html (last consulted August 2012)

[16] This terminology points towards acknowledgement of uncanny biological properties and a sense of the sacred which permeates the language and structure of the contemporary biological science. This is especially evident in terms like sacrifice in the use of experimental animals (Lynch, 1988), in Haraway's (1997) analysis of oncomouse, and in public discussions of biotechnology (Davies, 2006). However, in this case the term was seemingly used ironically, inserted into quote marks by respondents themselves, deliberately undercutting the sense of the spectacular it would otherwise entail.

[17] The MGI E-mail List Service (last consulted September 2011) URL http://www.informatics.jax.org/mgihome/lists/lists.shtml

> ‘I supposed that I had accidentally bred a line where it was possible for a male pup to mature early and impregnate the female (pretty unlikely, but then so are virgin births)’. (Posting to MGI-LIST, 2008)

Others suggested that certain mutant strains might have alterations to their reproductive behaviour, which was not well characterised, such that females could delay the implantation of embryos after mating.

> ‘We’ve had this happen in our SKH hairless mice before. Although I don't think it's very common in most strains of mice used for laboratory research, there a number of mammals which have delayed implantation of embryos, which appears to be what happened in our case’. (Posting to MGI-List, 2008)

Yet others suggested there were rogue mice on the loose:

> ‘The explanations that I received from listeners were that rogue male mice loose in the room or facility could squeeze through amazingly small places, such as the hole where the automatic water tube enters the cage, and that mice had actually been witnessed copulating through a wire-top cage – apparently, they'll do anything necessary’. (Animal technician, by email, 2008)

Yet these kinds of biological emergence or lively exuberance were rarely valued. When I got back to the animal technicians to ask what they had done with these mice, the answer was always the same: ‘in all cases I euthanized the spurious litters’. At best, these unexpected mice were seen as tangential to the primary focus of research and the main task of providing standardised inbred animal strains. As another respondent suggested, these mice were ‘an unexpected puzzle that was not primary to my typical research ... would love to talk more about it with an expert on mouse reproduction, though’. At worst, these animals were disruptive to technological procedures directed towards producing mice as technical objects. I asked one respondent why these were not investigated further, and he replied,

> ‘From a research standpoint, unscheduled births disrupt research when they make a breeder female unavailable at the desired time. I'm not going to risk the trust that people have placed in me to provide the right genotype of mouse without fail or error

> when I can just euthanize the questionable ones and use only ones of which I'm personally confident'. (Animal technician, by email, 2008)

Collating these responses suggests the occurrence of unexpected litters might be more common than expected, but they seemed to be disposed of and any biological significance of the events downplayed. The work of the animal technicians and care staff in these facilities was organised to the production of undifferentiated experimental animal strains, to producing mice as technical objects. Labour in these sites is invested into the repetitive achievement of technical objects, rather than the potential for identifying new epistemic things. The animal's lively capacity for mutability is sidelined in the search for the human cause and solution.

> 'Whenever something strange happens in a mouse cage, the investigator blames the vivarium staff of carelessness, and the vivarium staff blame the investigators of not keeping adequate track of that they are doing'. (Animal technician, by email, 2008)

In one final exchange, I pushed further to ask: Does the fact that these sorts of surprises can still happen after about 100 years of working with lab mice ever change the meaning or challenge the outcome of the more routine experiments? They came back to me 'Am not sure about the last question...' At that point, the e-mail conversation ended. The mundane practices directed towards repetitively producing standardised mice did not allow the space to consider a different kind of encounter.

Vital differences and the deviance search

There are many similarities between these two narratives. Both are in centralised breeding facilities where mice strains are bred prior to experimental practices. All the animals embody the capacity to be modelled into standardised strains, as well as the potential for unexpected biological excess. The accounts could involve the same inbred strains of mice. In both instances, the staff involved in the day-to-day care of the animals are the ones who identify these biological emergences. In addition, in both instances, the unexpected discoveries raise discussion about the roles and relations between people, expertise, and animals in these sites. Yet, in the first context, the contingencies of biological vitality are celebrated. In the second, they are troubling or even denied. In the first, the animals can be reassembled into new epistemic things. In the second, they disrupt the smooth provision of

technical objects. The on site differences that influence whether these animal becomings constitute a new epistemic event or technical interruption are subtle. I suggest what is significant is the way each site is differently open to the wider international circulation of laboratory animals, to the potential for 'becoming worldly'. The location of the Jackson Laboratory enables the discovery of an unknown animal behaviour to be rearticulated internationally, via the research expertise, technical apparatus, data infrastructures and other projects around it. In the second, the materials, people, and practices are arranged only for the production of trustworthy, standardized animals of known genotype to more localised laboratories.

The movement of animals from one system to another, from technical object to experimental thing, can be considered quite literally. There are important differences in the institutional arrangements that facilitate or hinder this movement. The Jackson Laboratory is hybrid site, with large-scale facilities dedicated to breeding, maintaining and distributing inbred strains, physically alongside the laboratories for carrying out genetic research. It is partly funded by the scientific grants that support its research, and partly by its sales of inbred mice. This dual role gives it an unusually flexible position in relation to commercial laboratory animal suppliers, as it is partly funded by public money via the US National Science Foundation, and financial continuity in relation to university-based research facilities, as it has a recurrent income derived from mouse sales. This mix of research activities and animal provision means the mice do not have to travel far to move from being technical objects to epistemic things. This hybridity and recognition of animal mutability means that emergence is recognised as an ongoing inevitability at the Jackson Laboratory. To ensure the mice it distributes are standardized as far as possible, it carries out a regular deviance search. Any unusual animals are identified by animal caretakers, removed from breeding stock, and shifted to laboratories for investigation. Removed from breeding facilities, these moments of animal emergence are explored for their potential to become new models of human disease. Plasticity can become productive difference. '"What difference is there?" may always be transformed into: "what resemblance is there?" (Deleuze, 2004: 14). This biological resemblance is speculatively rearticulated with the range of human disorders they may be said to resemble, and new epistemic and financial opportunities emerge[18]. Sleep apnoea changes from being "bull-dog like" to being "mice-like," opening the way for new research into sleep disorders, potential therapeutic interventions and more sales of mice.

[18] Another research respondent rather disparagingly, but perhaps tellingly referred to this process as 'disorder shopping'.

The deviance search assures both the repetition and development of forms at the same time; animal becomings are linked to the processes of 'becoming worldly', or the potential affirmative reopening of a concept through repetition we find in Deleuze (2004; see also Bearns, 2000).

At many other sites, the specialisation of scientific research and commercial breeding facilities means there is an increasing gap between breeding and experimentation. Scientific researchers are increasingly trained in research specialisms, such as molecular biology or bioinformatics, only rarely encountering the animals in their education or research. The animals' care is overseen by animal caretakers, procedures carried out by animal technicians, and data transferred to principal investigators for analysis. Standard animals are imported from commercial suppliers or the Jackson Laboratory, and local colonies maintained on a budget to deliver only the expected animals for experimentation. The animal's biological emergence is excessive here. It is disruptive to the role of the laboratory mouse as a genetic tool, and to this local experimental use of a globalised technical object. Smaller animal facilities no longer have the resources to search for the telltale signs, the mice sleeping standing up, that may indicate spontaneous mutations or new behaviours. One rack of black or white mice looks much like any other to the quick health check. Yet, when unexpected litters appear, these cannot be ignored. By opening up uncertainty over the processes of repetition, these virgin births challenge assumptions of the stability of mice as technical objects. At the point of breeding, plasticity points to a potential collapse of repetition into uncontrollable difference, the spaces of standardisation fold into those of emergence, challenging the meaning of each; a 'becoming unworldly' perhaps, or a moment of Derridean deconstruction of the very possibility of repetition itself (Derrida, 1988; Bearns, 2000).

Conclusions: 'becomings belong to geography'

Despite the centrality of decontextualisation and universalisation to the epistemic claims of laboratory science (see Kohler, 2002), and the attention given to standardisation in the histories of model organism research, such processes are and can never be complete. The historical contingencies that have led to the assemblage of particular research activities in different locations, and the specific mix of epistemological, institutional, and economic imperatives at different sites mean that place still matters to science. In particular, in this paper, I have explored how the historical trajectories of research animals, whose genotype

and phenotypic forms are less standard than might first appear, intersect with the spatial relations at research sites, which shape whether emergent biological capacities constitute an opportunity or an issue. The processes of standardisation and the potential for becoming something different have been managed throughout the historical development of standardised strains with consequences for their geography. Indeed, geographical specificity is meant to be written into the full nomenclatures used to designate in-bred mouse strains. The commonly used C57Black6 mouse is not everywhere and always the same. It has sub-strain differences, such that the C57Black6J, held at the Jackson Laboratory, is slightly different to the C57Black6NJ, developed at the NIH and now available via the Jackson Laboratory[19]. The final letters are the laboratory codes that acknowledge the originary points of these universalised strains; but, they are rarely used in their entirety and these geographical suffixes are frequently forgotten. With post genomics comes growing recognition of the complex links between movement and repetition and that 'becomings belong to geography' (Deleuze and Parnet, 1987). Yet, the importance of geography raises further questions for generalising any links between social theory, biological practices and narratives of becoming. Specificities matter. In accordance with Donna Haraway, I would argue 'becomings with' are critical considerations here, precisely because, unlike 'becomings' they are instantiated 'in materialsemiotic places (here, not there; there, not here; this, not every-thing; attachment sites, not case studies for the general; oxymorons, not examples)' (2010, 53). To talk of 'becomings with' is not to be naïve about the power relations involved in laboratory research, but to stress its complex choreography and cartography.

Spatial differences are becoming more evident and important, as biomedical research becomes increasingly global in scope and newly attentive to the post genomic in practice (Leonelli and Sunder Rajan, forthcoming; see also Petryna, 2009). The potential for collective analysis though systematic reviews of the literature, or for international cooperation through shared repositories for mutant mice, is thwarted if subtle differences in mice forms are not recognised in experimental practices, or noted in formal publications. These spatial and biological differences also influence the position of newly emerging centres of laboratory animal science and supply, even as biomedical research becomes increasingly international. New sites of biomedical research and innovation, such as Singapore, find themselves locked into the use of these standardised, but also mutable

[19] For a description of the differences between these sub-strains, see http://jaxmice.jax.org/strain/005304.html (last consulted August 2012).

animals; their animal houses needing constant resupply from the Jackson Laboratory or other established stock, historically situated in Europe or the USA, if their research findings are to find a place in international journals. Meanwhile, the hybrid identity of the Jackson Laboratory, co-locating both experimental provision and practices within its facilities, means it continues to expand from its base in Maine USA, to new sites in Sacramento California, and now to proposed facilities in Florida and Connecticut too.

Spatial differences are also of central interest to the practices of the post genomic sciences. Compared to the apparently context-free coding functions imagined of early genetics, with its emphasis on biological contexts and epigenetic environments, post genomics turns out to have an explicitly spatial component. These different spatial dimensions are increasingly the focus of research and elaboration. Rather than seeking recourse to further standardisation (Richter et al, 2009), the challenge that comes with post genomics is to open up and understand the spatial processes involved in making and moving inbred strains. Yet precisely what, if anything, is opened up in each site needs careful attention; at present, there are what Michael identifies as an 'ironic spatialities', in which 'multiple and contrasting heterogeneous orderings (and disorderings) are co-present' (Michael, 2009: 88).

In this paper, I have explored the different (disordering) logics of biological excess evident in narratives of mutant mice and virgin births. Some moments of 'becoming otherwise' do draw attention to an animal liveliness, which is surplus to their role as technical objects, and is part of the differential reproduction of experimental systems. However, it would be a mistake simply to identify these disruptions as points from which to resist the "subjection of the living to the inhuman practices of modern organized capital" (Brown, 2006:332, see also Law, 2010, Braun, 2008). As Melinda Cooper (2008) points out, the expropriation of 'life as surplus' is an important component of neoliberal bioeconomies. There is a kind of Marxian surplus recuperated in these stories of mutant mouse discovery, which connects animal becomings to the potential for 'becoming worldly' through commodification practices. We might identify this in the quick speculation about novel genetic understandings of human disease and the scale of markets for new therapeutic interventions, which follow the simple empirical observation of one mouse found sleeping standing up. The processes of 'becoming with' here is directed towards human ends, even if these biological potentialities are now seen as more open than in earlier genetic imaginaries. It is, at the same time, a process limited to a few well-resourced and well-articulated research sites, which are able to author and amplify these new narratives of model development.

Elsewhere, it is the institutional, economic, and biological practices which maintain biotechnological assemblages in place that dominate. The management of biological surplus happens off-stage, in facilities which are directed towards the routine task of supplying genetically identical inbred animals. Here animals becomings are experienced as a more Nietzschian surplus, which is not necessarily 'in excess of' the standard, but rather 'of a different order from' it. These 'becomings' are so divergent from the expected biological outcomes that they cannot be articulated. Instead, they are denied. These moments are marked by the rapid turn to euthanasia, disconnecting the animals' potential to amplify processes of 'become unworldly' in sites that valorise genetic control. These are moments where there could be the potential for new biological understandings, but they remain unexamined. Any account of the relational affective and corporeal capacities through which we 'become with' mutant mice has to consider the denial of this surplus, and its implications for both human and animal lives. Even if there is an increasing openness to biological emergence in some sites, it remains dependent upon silencing the vitality of matter in others. The two kinds of surplus are connected. The work to articulate experimental assemblages, to make matter speak, is equalled by the work done to keep matter silent, heralding what Wynne (2005) identifies as the potential for reductionist returns. These narratives of becoming with mutant mice point towards the strategies and sites that articulate or deny emergence. These spaces matter, but so do the gaps between them. The empirical story ends with a lack of enquiry, an absence of interest in what might be left out: 'Am not sure about the last question... '. This final breach is not the opening up of biological possibility and ethical creativity, but rather tells of the routine time and animal lives spent in providing the right genotype of mouse without fail or error, for mice which are always already on the move.

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Acknowledgements

This paper arises from a research fellowship funded by the UK Economic and Social Research Council on 'Biogeography and Transgenic Life' [grant number RES-063-27-0093]. I am indebted to everyone who shared their experiences of working with mutant mice with me during this research. Preliminary versions of this paper were presented at the RGS/IBG annual conference in London (2008), in a session on 'Where species meet and mingle', at EASST/Society for the Social Studies of Science annual meeting in Rotterdam (2008), in the panel on 'Standardizing, Controlling, and Understanding the Mouse in Biomedical Research' and to the Experimentality seminar on 'Experimental Objects' at Lancaster University (2010). I am grateful for the formative comments and discussion at these events. My thanks to Mara Miele and Joanna Latimer for the invitation to participate in this special issue and to the reviewers for their insightful comments. I would like to thank Bruce Braun, Mike Michael, Richard Milne and Kaushik Sunder Rajan for engaging with and encouraging the experimental ideas that finally took form in this paper.