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The biosocial genome?

Interdisciplinary perspectives on environmental epigenetics, health and society

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In recent years, research on how the human environment and lifestyle influence gene expression has generated considerable scientific and public interest. Articles in prominent international newspapers with headlines such as "Why your DNA isn't your destiny" (*Time Magazine* in 2010) or "Poverty leaves traces in children's genome" (*Süddeutsche Zeitung* in 2016) have drawn public interest to the emerging field of environmental epigenetics. It is a subdivision of the much more heterogeneous research field of epigenetics, which aims to understand how interactions between the environment and the genome can lead to epigenetic modifications that affect gene expression. Environmental epigenetics is often heralded as providing a revolutionary perspective on disease aetiology, particularly with regard to so-called lifestyle diseases such as cardiovascular disease or diabetes. It is also often presented as a vital new framework for understanding differences in the susceptibility and resilience to mental illness and the long-term damaging effects of a wide variety of environmental factors.

Environmental epigenetics engages with the social context of both individuals and populations. Studies investigate, for example, how socio-economic status, exercise habits, diet or experiences of trauma might influence biological processes at the molecular level. This has created great interest among social scientists and scholars in the humanities as it raises a number of questions at the intersection of the natural sciences, the social sciences and the humanities: for example, how to conceptualize the social environment in a laboratory context. To explore research areas at these intersections and assess the potential social and political implications of environmental epigenetics, international scholars from the life sciences, social sciences and humanities met in January 2017 in Munich, Germany. This article presents some of the main findings from these interdisciplinary discussions. We conclude that environmental epigenetics has great potential for elucidating how human society affects human biology, but we caution against over-simplified translations from social structures to biological processes and *vice versa*.

Genes and their environments

Traditionally, epigenetic research has been mostly concerned with understanding the basic mechanisms of cell differentiation and cell identity. However, in the public arena studies from environmental epigenetics have often come to stand in for epigenetics research as such. This has been due to a number of provocative propositions that have caught the attention of the wider public and scientists alike. Environmental epigenetics proposes that the environment—including both material and psychosocial factors—might play a much more important role in gene regulation and expression, and thereby for health and illness, than was previously assumed [1]. Studies in environmental epigenetics have explored, for example, the effects of air pollution, pesticide exposure, physical exercise and emotional stress on

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the epigenome. Some studies focused on the potential effects on adult health, whereas others highlighted the potential long-term effects of such exposures during prenatal and early postnatal life. Such studies have been particularly prominent in the public domain as they concern, for example, how maternal nutrition or early-life stress affects the epigenome of the offspring to increase the risk of chronic disease or behavioural problems later in life. Here, environmental epigenetics is in close conversation with research on the Developmental Origins of Health and Disease (DOHaD), which explores how events during early development can shape health or illness later in life [2]. Other, often controversial, lines of research concern how environmental effects could be passed on across generations via epigenetic modifications, in a manner reminiscent of Lamarckism.

"Environmental epigenetics engages with the social context of both individuals and populations"

While studies in environmental epigenetics might help to account for the impact of environmental exposures and experiences on health, there are certain limitations. Many of the fundamental studies have been conducted in rodents, which raises questions about the validity of extrapolating the results to humans. Studies in human cohorts and patient groups in turn are often limited by the availability of appropriate samples, as epigenetic processes are mostly tissue-specific: peripheral blood cells may not reflect epigenetic changes in, for example, the brain or the liver. Furthermore, the cost of analysing epigenetic changes is still high, and replicating findings across human cohorts or patient groups remains challenging. Many studies that report epigenetic changes in human tissue in response to environmental factors do not demonstrate any functional or physiological effects. Moreover, epigenetic changes range from DNA methylation to histone modifications to non-coding RNAs. Even DNA methylation, the most intensely studied modification, can yield highly complex patterns that influence gene expression in many different ways. Finally, there is increasing evidence that interactions between epigenetic effects and genetic changes play an important role, too. Given these complexities, epigenetics creates considerable challenges for bioinformatics to yield meaningful results, arguably to an even greater extent than studies of genetic variations alone.

Despite these limitations and the significant controversies around certain claims—such as transgenerational inheritance of epigenetic changes—there are several reasons why a more detailed consideration of the social and political dimensions of environmental epigenetics is now timely. First, its findings circulate widely not only in academic research, but also in the media, where it is related to social phenomena such as the so-called obesity epidemic, the mental health status of refugees or the possible inherited effects of trauma. Second, research findings from environmental epigenetics might affect policy in areas such as public health and environmental and social policy: some argue that this is already apparent in recent UK policy documents on the effects of poverty on childhood development [3]. Third, environmental epigenetics can be seen as an instance of a wider shift in the molecular life sciences towards what has been described as a "postgenomic" perspective, which considers biology as plastic and open to environmental processes as opposed to being determined by inherited genetic influences [4]. This opens up novel opportunities for collaboration between researchers in biology, the social sciences and the humanities.

Biology and society

Researchers from the social sciences and humanities have already been engaging with environmental epigenetics for a while. Research perspectives with a stronger focus on the role of the environment in health and disease constituted a welcome move away from studying the role of genes in isolation. This shift resonated with findings from the social sciences that social contexts shape patterns of health and disease. From this perspective, two features of environmental epigenetics stand out as particularly promising for providing insights into the relationship between social experiences and biological processes. First, environmental epigenetics is predicated on the concept that the body is open to environmental influences. Much of the environment in which humans develop and live is the result of human activity itself, such as the quality of food or housing. In this sense, environmental epigenetics is open to social and political questions from the outset. Highlighting the fact that the development of health and disease is often mediated by social factors, it points to new ways of conceptualizing the extrinsic factors associated with health inequalities in fields such as toxicology or mental health research.

Second, environmental epigenetics proposes new ways of thinking about the temporal dynamics of health and disease across the life course of an individual and even across generations. In particular, the hypothesis of so-called critical windows of development in prenatal and early postnatal life, during which environmental influences such as nutrition, toxins or trauma can affect later life health outcomes, raises questions for public health in terms of how to better address unjust living conditions that might limit an individual's ability to improve their health and that of their children.

". . . environmental epigenetics proposes new ways of thinking about the temporal dynamics of health and disease across the life course of an individual and even across generations"

It is important to note that this emphasis on the influence of the environment on phenotype is not a new proposition or a radical new perspective in biology. Environmental epigenetics is part of a long history of negotiating the relationship between the environment and the body, a theme which even Aristotle already explored in his theory of embryonic epigenesis. The idea that environmental influences could "damage" biology was also central to the emergence of public hygiene and social medicine movements during the 19th century. Conversely, it played a key role in concerns about "degeneration", which focused on how the living conditions of industrial societies might affect the hereditary material of nations and so-called races; such concerns culminated in the eugenics movements of the early 20th century that sought to limit the reproduction of those deemed biologically inferior [5]. From a historical point of view, the focus on

the gene as a primary determinant of development and the associated separation of biology and society has been the exception rather than the rule. In considering the potential and the challenges of environmental epigenetics, it is therefore important to keep in mind the long history of ideas about the relationship between biology and the environment, and their complex socio-political implications.

> *"...deterministic readings of epigenetics [...] may create the impression that individuals, their health and their behavior are bound and ruled by the epigenetic marks they have acquired in early life"*

Considering the social and the biological as strongly connected creates numerous opportunities and challenges for contemporary science and society. In our workshop, we identified three challenges in particular that merit closer attention.

Experimental reductionism and the exclusion of social complexity

Environmental epigenetics tends to locate the development of health and disease primarily at the level of individuals, at the expense of more structural views that encompass social, political and economic determinants of health. This may appear paradoxical as, after all, environmental epigenetics concerns how *environmental* factors affect gene expression. However, much depends on exactly how the environment is defined and conceptualized within research—and there are factors that might lead to a narrow understanding of the environment in epigenetic research.

Experimental studies on the epigenetic effects of "maternal care" offer an illustrative example. Here, the work of Moshe Szyf, Michael Meaney and colleagues [6] has become iconic. In a series of experiments, they investigated the programming effects of maternal behaviour on offspring in rodents, showing that the degree to which dams lick and groom their pups—what the researchers called "maternal care"—changes the epigenetic profile in the hippocampus of their pups. Offspring that had been licked and groomed less frequently showed reduced expression of the glucocorticoid receptor gene, while frequent licking and grooming had the opposite effect. The researchers argue that the behaviour of the dam altered stress responses in her pups and induced more anxious behaviour in those pups which received less "maternal care". These experiments are foundational to a strand of research that explores the epigenetic effects of early-life stress, deprivation and trauma in rodent model organisms.

In media presentations and in the peer-reviewed literature alike, these experiments are frequently related to how the behaviour of human mothers influences the psycho-physical development of their children. Two aspects are particularly striking about this translation. The first is how seamlessly findings from rat experiments are transposed into human contexts. This has been achieved by comparing epigenetic studies in rats to selected psychological studies in humans without adequately discussing species-typical behaviour, developmental differences or any reference to controversies about the interpretation of these studies within their own fields [7]. Second, it is remarkable how isolated the figure of the mother often appears. Basic research requires control of experimental conditions to permit verifiable interpretation. But this can be problematic if it excludes important factors as potentially confounding or contributing variables. For example, in exploring the hypothesis that maternal behaviour shapes the epigenetic profiles of rat pups, factors such as peer relations or the role of fathers—important in humans but not rats—are not considered. When these experimental findings are transposed to humans, the discussion about the importance of optimizing maternal behaviour tends to ignore other factors that shape child development and the lives of mothers, but which may be beyond their control.

This tendency to narrowly generalize from the experimentally controlled conditions of research using animal models to more complex human contexts is also illustrated by research on the intergenerational aspects of childhood obesity, which has become a major public health concern. Most research in this area focuses on how maternal body weight, nutrition before and during pregnancy, and the child's food during the early years might induce a propensity for obesity via epigenetic mechanisms. Many of these studies use socio-economic status (SES) as a variable in their study design to report associations between higher body weight and poor nutrition in low-SES mothers, both of which have been labelled as risk factors for childhood obesity. Given this focus, discussions of possible interventions often focus on educating mothers about how to eat better and lose weight before pregnancy.

> *"Even if catchy metaphors like "programming" might attract attention to a new research field, [...] their social meaning and impact must be considered carefully"*

At the same time, we know that the risk of obesity and malnutrition is distributed unequally across society, with low-income individuals being particularly affected owing to reduced access to healthy foods (so-called food deserts) or lack of opportunity for physical exercise. Similarly, the ability to breast-feed can depend on SES and flexible working arrangements or extended maternity leave. The point is that, if we hope to translate the findings of epigenetic research on the developmental mechanisms linking nutrition with disease risk into effective health policy, it is imperative that we view nutrition not as a simple exposure in isolation, or a function of individual choice, but as a resource that is constrained in complex ways by social and structural factors that distribute resources, and chances of health, unevenly across society.

A focus on durability and the question of reversibility

Much research in environmental epigenetics concerns the phenotypic changes during development, or those operating during the early stages of disease. Even though these are circumstances when substantial phenotypic effects occur, there is a tendency in the life sciences towards a narrow focus on durable positive or, more often, negative epigenetic effects of environmental factors. This is evidenced by the widespread use of the metaphor of "programming" [8], which is misleading in that it implies that the phenotypic outcome is determined by a programme, rather than being affected by a

range of environmental factors over a sustained period. The related concepts of "critical" or "sensitive" windows, during which external environmental processes operate to change the phenotype, may also be unduly restrictive. For the development of neural systems, such as the visual cortex, such critical periods indeed take place during the neonatal period. Yet, most biological systems show a degree of plasticity and flexibility on a much longer timeframe—even contributing to the variation in the decline of function during ageing, for example.

As new research adds to the evidence for intergenerational, and possibly transgenerational, passage of epigenetic marks, it becomes necessary to consider the significance of environmental epigenetics across a range of timescales, from the development of an individual to the evolution of a species [9]. At every level on this spectrum, there has been much less research into plasticity and reversibility of epigenetic marks in contrast to the induction of epigenetic changes. The revival of Conrad Waddington's "epigenetic landscape" model has further reinforced simplified views of the gene/environment, nature/nurture dichotomies. While Waddington did indeed consider the canalization processes in this landscape as operating to restrict the effects of external influences on the genome, his model was in fact more holistic, with the "landscape" less a fixed entity and more a flexible surface like a tent, supported by poles and guy ropes attached to pegs. Any change in tension of one rope would produce shifts across the whole canvas. Thus, environments do not simply alter development by determining which epigenetic valley an individual enters, but by altering the conformation of the valleys themselves. We feel that this conceptualization better captures the ways in which social and cultural factors alter biological processes, life trajectories and health.

Deterministic reasoning and the risk of stigmatization

The two trends described above might interact to create another challenge as epigenetic reasoning enters broader societal discourse: the risk of social discrimination based on the assumption that certain individuals might be "epigenetically damaged" by their (early) life experiences or exposures. This is a topic that deserves specific attention as a range of studies in environmental epigenetics focus their attention on socially pre-defined subgroups in society, particularly adults and children in low-SES households, ethnic minorities or survivors of specific forms of early-life trauma. This focus may be expressed in a number of ways: in sampling these groups for cohort studies; using such attributes as variables in experimental designs; or explaining assumed group differences in human society through simple reference to findings in model organisms or through comparison of studies in model organisms with human studies in other disciplines. In this context, deterministic readings of epigenetics, as discussed above, may create the impression that individuals, their health and their behaviour are bound and ruled by the epigenetic marks they have acquired in early life. Such a perspective is problematic for a number of reasons.

For example, a British webpage about health during and before pregnancy, supported by researchers from a number of renowned universities and featuring epigenetics prominently, includes a video narrative about a young man recently released from prison (www.beginbeforebirth.org). His difficulties in school and working life and his criminal record are explained as potential outcomes of his mother's stressful pregnancy and her failure to provide enough "warmth" as a single parent in a tough living situation. "Charlie wasn't born a criminal", the narrator suggests, "but research suggests that his time in the womb and his early life could have made his behaviour more likely. [...] Maybe if Charlie's time in the womb had been different, he'd have been different, too".

Such simplified narratives—which are in no way supported by social or biological data—may easily stigmatize individuals who have experienced hardship in their early life, as they suggest that they tend towards socially problematic behaviours. Social justice activists in the USA, who advocate for reforms in the school and juvenile justice system, frame such a determinist perspective as one of the greatest dangers to successfully using novel biological insights for improving the situation of young individuals from difficult homes. They fear, for instance, that such renderings of what environmental epigenetics can say and know about human psychosocial development might already be contributing to the limited availability of parents willing to foster children from difficult households, since such a deterministic perspective suggests that they are "damaged" in lasting ways that could not be ameliorated by the foster family.

Representations of epigenetic findings on the effects of early stress, such as the above, commonly fail to recognize a significant body of relevant social science research, such as studies of social mobility and rehabilitation. This literature points to

Sidebar A: Studying Science, Technology and Society

Many of the authors of this article are located in the interdisciplinary field of Science and Technology Studies (STS) or in related fields, such as philosophy, history, sociology or anthropology of science. STS is the study of how social, political and cultural values and structures affect research and technological innovation, and how research and innovation in turn affect society, politics and culture. STS scholars study not only how scientific knowledge is produced, but how it is embedded in specific social, political, economic and historical contexts. For example, research on the historical relationship between eugenics, biology and culture has informed questions about genetic and genomic research. How does this research draw on, relate to and produce categories of human differences, and what social and political effects does it have?

STS scholars studying environmental epigenetics have explored how researchers design their experiments and studies, how they turn the complex category of "the environment" into measurable variables, how they make equivalences between humans and model organisms, and how their research challenges, builds on or transforms the key intellectual frameworks of genetics and genomics. They have also studied how claims about environmental epigenetics are taken up in the popular media, in science policy and by researchers in other fields. Finally, STS scholars have investigated how narratives and metaphors emerging from environmental epigenetics shape understandings of gender, race, class and sexuality, together with social experiences such as trauma, deprivation, racism and war (see Sidebar B). They are increasingly participating as collaborators in research fields like genetics, neuroscience or environmental epigenetics, contributing their expertise on the social, political, historical or philosophical dimensions of science to the design of research questions and experiments and the interpretation of studies. In some universities, STS is also gradually becoming part of life science and other natural science curricula, giving these students the opportunity to acquire critical skills for understanding the complex relationships between science and society.

Sidebar B: Further reading

For an overview of environmental epigenetics and the developmental origins of health and disease see:

- Feil R, Fraga MF (2012) Epigenetics and the environment: emerging patterns and implications. *Nat Rev Genet* **13**: 97–109
- Hanson MA, Gluckman PD (2014) Early developmental conditioning of later health and disease: physiology or pathophysiology? *Physiol Rev* **94**: 1027–1276

For an introduction to how the social sciences, the humanities and biology might benefit from interaction and collaboration around environmental epigenetics see:

- Pickersgill M, Niewöhner J, Müller R, Martin P, Cunningham-Burley S (2013) Mapping the new molecular landscape: social dimensions of epigenetics. *New Genet Soc* **32**: 429–447
- Singh I (2012) Human development, nature and nurture: working beyond the divide. *BioSocieties* **7**: 308–321

For a deeper understanding of the entangled history of eugenics, the biology of heredity, politics and culture see:

- Meloni M (2017) *Political biology. Science and social values in human heredity from eugenics to epigenetics*. London and New York: Palgrave
- Hanson C (2012) *Eugenics, literature and culture in post-war Britain*. Abingdon: Routledge

For a critical discussion of the relationship between epigenetics and categories of social difference such as race, class and gender see:

- Kuzawa CW, Sweet E (2009) Epigenetics and the embodiment of race: developmental origins of US racial disparities in cardiovascular health. *Am J Hum Biol* **21**: 2–15
- Mansfield B, Guthman J (2014) Epigenetic life: biological plasticity, abnormality, and new configurations of race and reproduction. *Cult Geogr* **22**: 3–20
- Niewöhner J (2011). Epigenetics: embedded bodies and the molecularisation of biography and milieu. *BioSocieties* **6**: 279–298
- Hanson M, Müller R (2017) Epigenetic inheritance and the responsibility for health in society. *Lancet Diabet Endocrinol* **5**: 11–12
- Kenney M, Müller R (2017) Of rats and women: narratives of motherhood in environmental epigenetics. *BioSocieties* **12**: 23–46
- Richardson SS, Daniels CR, Gillman MW, Golden J, Kukla R, Kuzawa C, Rich-Edwards J (2014) Don't blame the mothers. *Nature* **512**: 131–132

For a study of the emerging metaphors and language of environmental epigenetics in scientific and popular writing see:

- Stelmach A, Nerlich B (2015) Metaphors in search of a target: the curious case of epigenetics. *New Genet Soc* **34**: 196–218

For a reflection on the broader changes in the intellectual frameworks of biology in the so-called postgenomic era see:

- Richardson SS, Stevens H (eds) (2015) *Postgenomics: perspectives on biology after the genome*. Durham: Duke University Press

the importance of taking into account the effects of macro-economic structures, social relations in later life and opportunities afforded to disadvantaged individuals by different social institutions [10]. A failure to acknowledge the greater complexity of social life might lead environmental epigenetics to contribute, possibly unwittingly, to perspectives that frame poverty and social disadvantage as something that "replicates itself from generation to generation" through —as one Op-Ed in the New York Times put it—individual "brain architecture" rather than social conditions that are and can be crucially influenced by social and economic policies (http://www.nytimes.com/2012/10/21/opinion/Sunday/kristof-cuddle-your-kid.html?_r=0). It might also lead to further stigmatization of individuals who had to flee war and oppression, and seek a new life in other parts of the world. This might create the opposite effect of what many researchers in environmental epigenetics hope to do: to contribute to positive social and medical change by rendering the embodied effects of unjust living conditions biologically visible. However, such a project might require greater interdisciplinary sensibilities in order to avoid the pitfalls of determinist and potentially stigmatizing perspectives.

Conclusions

As researchers in environmental epigenetics and other fields in biology come to engage more with the social world and its effects on the body, health and disease, the social and political dimensions of their work inevitably become apparent. We suggest that they need to engage more actively with these matters in order to remain accountable for how their work contributes to certain visions of society and not others. Environmental epigenetics holds the potential to help us better understand how social inequality and other factors contribute to health and illness and can help focus social policy to achieve societal improvements. However, it can also be the basis for assigning undue blame to disadvantaged individuals or for increasing stigmatization.

How can we address this ambivalent potential responsibly? One important way is through interdisciplinary conversation and collaboration. Various authors of this commentary have begun to collaborate to bring social science insights into the complexity of social life and life science findings about epigenetic mechanisms to bear on novel experimental designs. Sarah Richardson and Heather Shattuck-Heidorn at Harvard University, for example, collaborate across the disciplines to study how not only physical sex differences, but also gendered life experiences, such as role expectations or sexism, shape differences in disease risk between men and women.

As biological research comes to address social issues and categories in experimental designs, it is important to recognize that expertise on social processes and structures is limited in biology. Hence, it is crucial that biological research draws on relevant expertise from the social sciences and humanities, which can help to refine the formulation of research questions and interpretations of results. Systematic reflection is also important regarding the language that is being used to report novel findings. Even if catchy metaphors like "programming" might attract attention to a new research field, and claims about the relevance of ongoing basic research to human health and society can be important for acquiring funding, their social meaning and impact must be considered carefully. This implies a responsibility for funding bodies to reward cautious claims rather than overstatements and to support interdisciplinary collaborations that allow

for sensible approaches to these important research topics. This is particularly crucial given the at times troubled histories of scientific claims about the relationship between social structure and biology and the ways in which accounts of human difference can contribute to social stratification and discrimination.

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Conflict of interest

The authors declare that they have no conflict of interest.

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7. Kenney M, Müller R (2017) Of rats and women: narratives of motherhood in environmental epigenetics. *BioSocieties* 12: 23 – 46
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9. Kuzawa C, Thayer Z (2011) Timescales of human adaptation: the role of epigenetic processes. *Epigenomics* 3: 221 – 234
10. Buffone S (2012) Towards an integrative theory of crime and delinquency: re-conceptualizing the Farrington theory. *Int J Criminol Sociol Theory* 5: 895 – 911

