

*Troubled by Heterogeneity?: Control, Infrastructure and Participation in the Study of Heredity
and STS*

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Preamble:

Much of my interdisciplinary work is informed by what I call "reciprocal animation":
Close examination of conceptual and methodological developments within the sciences
can lead to STS questions about the social influences shaping scientists' work or its application,
which, in turn, can lead to new questions and awareness of alternative approaches in those
sciences.

Introduction:

The two foundational developments of modern biology—the theories of evolution by natural
selection and the genetic basis of heredity—were built from language, arguments, evidence, and
practices of controlled breeding in agriculture and the laboratory.

The relationship between variation, particularity, or, more generally, heterogeneity and control
provides an under-developed angle from which to view modern understandings of heredity and
development over the life course.

Argument:

My guiding contention is that research and application of resulting knowledge are untroubled by
heterogeneity to the extent that populations are well controlled.

Such control can be established and maintained, however, only with considerable effort or social
infrastructure, which invites more attention to possibilities for participation instead of control of
human subjects.

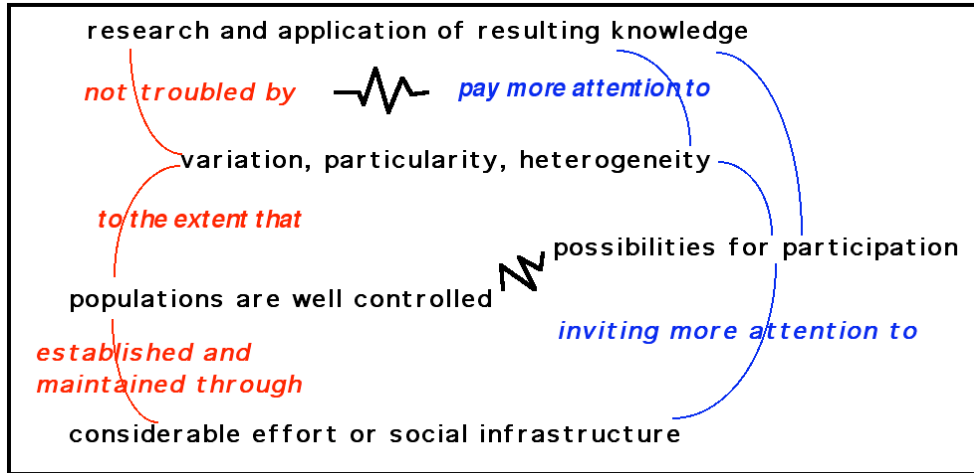


Figure 1. Schema of the paper's contention, applying both to the modern understandings of heredity and to STS interpretations of science. (Zig-zag lines indicate a tension or contrast)

This framework will be introduced through vignettes from genetics and epidemiology, then its extrapolation to STS considered.

1. Responding to genetic conditions requires social infrastructure(s)

The man of the moment [was] J. Craig Venter, Ph.D., whose pioneering work to sequence the human genome — our essential code for life — had whetted public appetite for medical miracles in the diagnosis, treatment and prevention of even the most complex of common diseases. "Imagine a world where families leave the hospital with their newborns and take their baby's complete genetic profile with them on a CD-ROM," Venter told his audience. "And imagine a world where your physician has as part of your medical record your genetic code, which can be used to determine, for example, your risk profile for side effects from drugs or other medical treatments. These might be possible in a genomics-based medical system in the near future." (Massoglia 2003)

"Imagine a world..." If the case of phenylketonuria (PKU) is any guide to our imagination, significant complexities should be expected to arise if neonatal genetic diagnosis and advice about risks and possible protective measures become widespread. Until the 1960s people with two PKU genes always suffered severe mental retardation. But now the brain damage can be

averted by a special diet free of the amino acid phenylalanine following detection of those newborns having high phenylalanine levels.

Yet, as Diane Paul's (1998) history of PKU screening describes, the certainty of severe retardation has been replaced by a chronic disease with a new set of problems. Screening of newborns became routine quite rapidly during the 1960s and 70s, but there remains to this day a struggle in the USA to secure health insurance coverage for the special PKU diet and to enlist family and peers to support PKU individuals staying on that diet through adolescence and into adulthood. Moreover, for women who do not maintain the diet well and become pregnant, high phenylalanine levels adversely affect the development of their non-PKU fetuses; such "maternal PKU" is a public health concern that had not previously existed.

PKU is often invoked to claim that genetic does not mean unchangeable. This picture is too simple. PKU individuals are subject to heterogeneous influences on their pathways of development over the life course. A more complex picture involves questions about control and social infrastructure and opens up possibilities for participation: Who is responsible if a baby is diagnosed with PKU, protective measures are not taken or are not sustained, and the child becomes a retarded adult or mother of a child with maternal PKU? Anyone wanting to improve the lives of PKU individuals needs to consider where they are prepared to get involved—Would the best point of engagement be around reduction in false positives or negatives? Diagnosis of variability in effects of exposure? Personal motivation and understanding of people with some mental deficits? Support groups for individuals and families? Insurance coverage for the special diet and for counseling? Paid family leave, or...? The possibilities for participation are diverse, depending on how people who want to help—which may include scientists and STS interpreters of science—can build or adjust the relevant social infrastructure (Taylor 2009).

In short, the common claims that molecular biology and biotechnology will allow genetic information to reshape human life are fantasies in contrast to the idea that, in practice, many diverse materials, tools, and other people have to be engaged to realize any enduring result (Robinson 1984).

2. Social infrastructure is implied by knowledge about gene by environment interaction

In 2002 Avi Caspi, Terrie Moffitt and colleagues published two articles in *Science* that examined psychological traits in relation to measured genetic and environmental factors. One of them reported on anti-social behavior in adults in relation to the activity of monoamine oxidase type A (MAOA) and childhood maltreatment; MAOA deficiency was a strong predictor of aggressive behavior only when the child had also been maltreated.

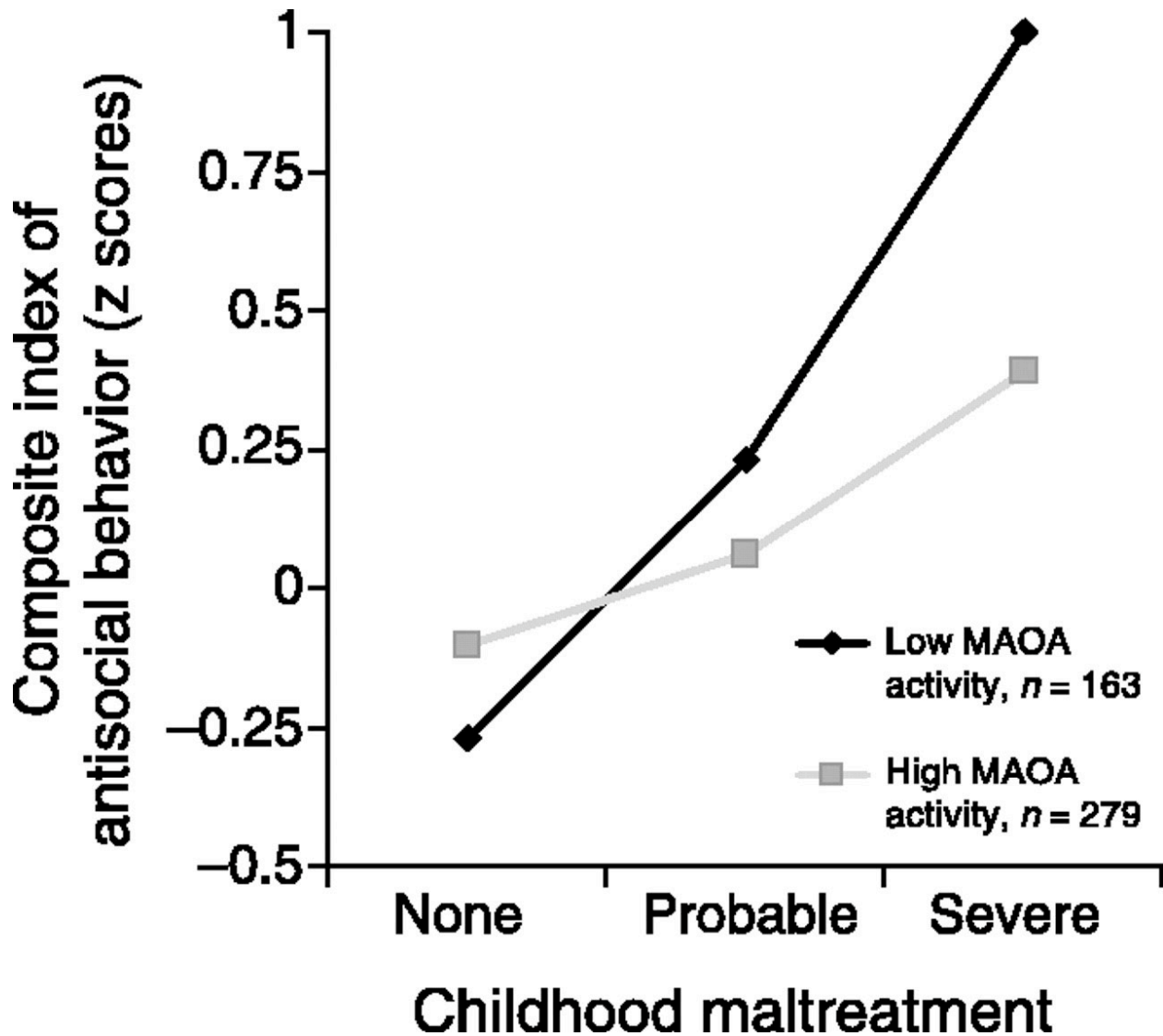


Figure 2. Means on the composite index of anti-social behavior as a function of MAOA activity and a childhood history of maltreatment (from Caspi et al. 2002, 852).

The authors conclude that their results "could inform the development of future pharmacological treatments" (Caspi et al. 2002, 853). In the context of research on childhood experiences in relation to adult behavior, the implication is that, if low MAOA children could be identified, prophylactic drug treatment could reduce their propensity to anti-social behavior as adults.

An easy rejoinder would be that, if *childhood maltreatment* could be identified and stopped early, this action could reduce a child's vulnerability to low MAOA levels and undesired adult outcomes. Indeed, eliminating childhood maltreatment would seem to be unconditionally positive, while prophylactic drug treatment may have side-effects; some of these might not emerge till many years have passed.

The rejoinder is too easy, however. The social infrastructure needed to detect and prevent childhood maltreatment would intrude into many households, require surveillance, monitoring, and intervention by state agencies, divert government budgets from other needs, and so on. Reduced childhood maltreatment may be a positive outcome, but the *means* are not unconditionally positive to all—How would decisions about investment in the social infrastructure be decided? How would individuals decide where to engage with that social infrastructure once it is established? (These questions can be raised about the gene by environment interaction research program even though some meta-analyses have cast doubt on the generality of the specific 2002 Caspi and Moffitt results; Risch et al. 2009.)

Vignette Part B.

An examination of variation of outcomes within the genetic and environmental categories (e.g., low/high MAOA and no/probable/severe childhood maltreatment) and its implications for the idea of early detection and intervention on the basis of MAOA status (building on Taylor 2009). Among children who experienced probable or severe maltreatment, the ranges overlap, that is, some of the high MAOA individuals ended up with higher anti-social behavior scores than some of the low MAOA individuals.

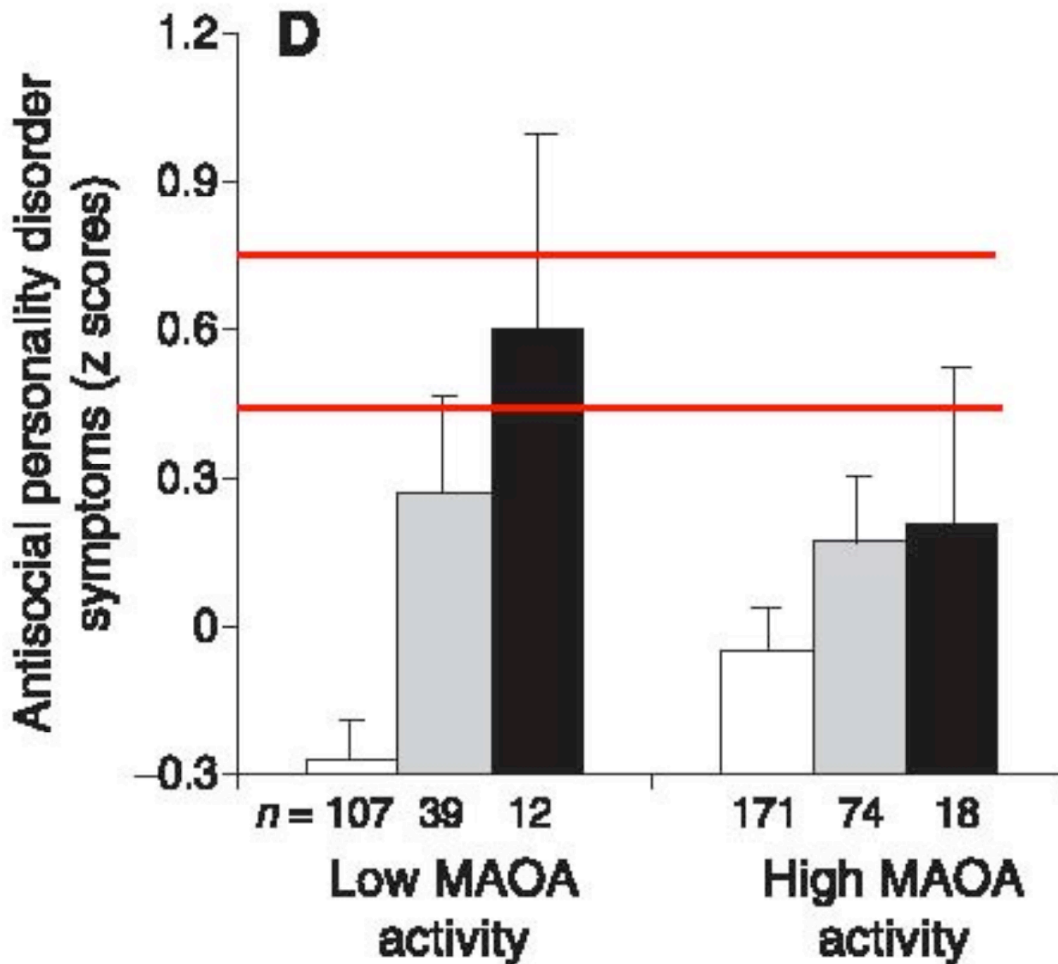


Figure 3. The association between childhood maltreatment and subsequent antisocial behavior as a function of MAOA activity (from Caspi et al. 2002, 852). The blank, gray, and black columns depict, respectively, no, probable, and severe maltreatment. The horizontal lines are added by the author (see discussion of the effect of adjusting what counts as antisocial).

The potential for misclassifying children in or out of the category of people who may end up antisocial is not eliminated by adjusting what counts as antisocial. (If we count as antisocial, for example, only those individuals whose score exceeds some value that is higher than the upper limit of the range for high MAOA individuals, this increases the numbers of low MAOA individuals who do not end up counting as antisocial. If we lower the cutoff score, many high MAOA individuals end up with behavior classified as antisocial.)

The issue of misclassification could be troubling because, once the resources are invested to screen children for MAOA levels, attention would be focused on *all* low MAOA children. Indeed, *how could this stereotyping be avoided* if we do not know from a childhood MAOA assessment whether any particular individual is one who would go on, after childhood maltreatment, to become an antisocial adult?

Additional research would be needed to identify other characteristics that differentiate among the low MAOA children (and perhaps help predict who among the high MAOA children are also vulnerable). If that research were successful, additional resources would have to be invested to customize the way that parents, teachers, doctors, social workers treated the different low and high MAOA children and to educate everyone not to treat children according to their MAOA group membership.

In short, just as in the PKU case, the meaning of new genetic knowledge (in this case in combination with environmental knowledge) is contingent on the presence or absence of social infrastructure; the positive benefits depend on extensive control of human subjects.

3. The path to personalized medicine may run through social stereotyping

Suppose the MAOA example concerned not antisocial behavior but a less charged condition, say, some specific adult disease. *What kinds of medical conditions would receive the necessary investment in pharmaceutical and sociological research, screening, and preventative treatment/monitoring to address the conjunction of genetic and environmental factors involved?*

Some well-organized parental advocacy groups may secure funding to address the prenatal diagnosis and post-natal treatment of rare debilitating genetic disorders (such as PKU).

However, public and corporate policy would more likely focus on conditions for which the number of vulnerable people times the average benefit of ameliorating the effect of the genetic difference would be large.

In such cases, if the MAOA case is any guide, *if* the effect of the genetic difference depends on identified social or environmental factors, and *if* variability within the groups that have on-

average high and low vulnerability produces a problem of misclassification, pressure would arise for researchers to differentiate among individuals within the groups. Yet, until distinguishing characteristics were found, parents, teachers, doctors, social workers, insurance companies, policy makers, friends, and the individuals themselves could do no better than treat individuals *according to their group membership*. Indeed, if the additional research were not conducted or not successful, or if the cost of differentiating among individuals were too high, *we might never get beyond treating individuals according to their group membership*.

The scenario speaks to the prospect of personalized medicine. In its simplest form, personalized medicine involves the use of genetic information to predict which patients with a given condition (e.g., heart arrhythmia) will benefit from a particular drug treatment (e.g., beta blockers). More ambitiously, personalized medicine promises to inform people of their heightened vulnerability (or resistance) to specific environmental, dietary, therapeutic, and other factors early enough so they can adjust their exposure and risky behaviors accordingly. If the MAOA analogy holds, the path to personalized medicine will, ironically, pass through a phase in which large numbers of people are treated according to their group membership. Moreover, this phase may not be a passing one: What conditions—what social infrastructure—can ensure that the information and resources needed to move beyond it are forthcoming?

4. the relationships that STS scholars make between interpreting scientific projects and influencing their direction

It is routine in STS to portray scientists and engineers shaping society as they establish knowledge or make technologies work. The shaping of society involves building infrastructure (or implying that such infrastructure can be taken as given). Yet, to interpret science is also to make knowledge claims. So, STS scholars might reflexively ask what aspects of society we are trying to shape (Taylor 2005). After all, STS interpretations often suggest that things could be (or could have been) otherwise.

Are we envisaging then that our critical social/historical/conceptual interpretations will influence scientists? Would this happen *directly*, through contributions in scientific publications and meetings; *indirectly*, through science journalism and writing for a wider audience; or perhaps

over the long term, through STS-informed courses taken by some scientists-to-be? How do we decide whether and when to “go native” among the scientists in their labs or field sites or to become active citizens or consultants in policy debates? And so on.

Tensions around heterogeneity and control run through any such reflexive questioning of STS efforts to shape society. Decisions about what we want to do with knowledge depend on our particular situations as STS scholars and the ways these have evolved over our personal and professional life courses. At the same time, conventions and constraints of influencing an audience lead us to push to the background the *particularities of situatedness*—our own and the audience members.' There is a premium on claims that appear *general*, i.e., adoptable by others. *Subjectivity* in knowledge-making is played down in favor of the objective and reliable.

Then again, the audience in STS is familiar with the idea that *heterogeneous resources* are brought into play in establishing knowledge and making technologies reliable—scientists employ or mobilize equipment, experimental protocols, citations, the support of colleagues, the reputations of laboratories, metaphors, rhetorical devices, publicity, funding, and so on (Latour 1987, Law 1987, Clarke and Fujimura 1992, 4-5, Taylor 2005, 93ff). Yet this emphasis means that each case of science-in-process has its own particular, even idiosyncratic, complexity. To convey such complexity is to run the risk of our STS interpretations being intelligible only to the group of specialists interested in the particularities of the given case. STS scholars often, instead, acknowledge techno-scientists' efforts to control heterogeneous resources and actors, but then focus audience attention on key concepts concerning those efforts, such as Pasteur's laboratory as an "obligatory passage point" (Latour 1988) and the creation and management of "boundary objects" (which include concepts, tools, institutional arrangements) that many actors can employ in their particular social worlds without jeopardising the object's integrity (Star and Griesemer 1989).

We might, in light of this paper's overall contention, examine the social infrastructure that has grown around the invocation of such key concepts in STS. For this short paper, however, I want simply to note some possibilities for participation among, more than control of, audiences and other human subjects.

My formative experience as an agricultural and environmental researcher and activist led me in the late 1980s to suggest that anyone wanting to influence developments in some area of science might benefit having some kind of map of the complexity of resources or practical commitments involved in knowledge construction in their own area. Such maps expose multiple places at which concrete alternative resources could be mobilized, thus allowing a range of researchers to identify specific changes that they could effect given their own particular background and interests.

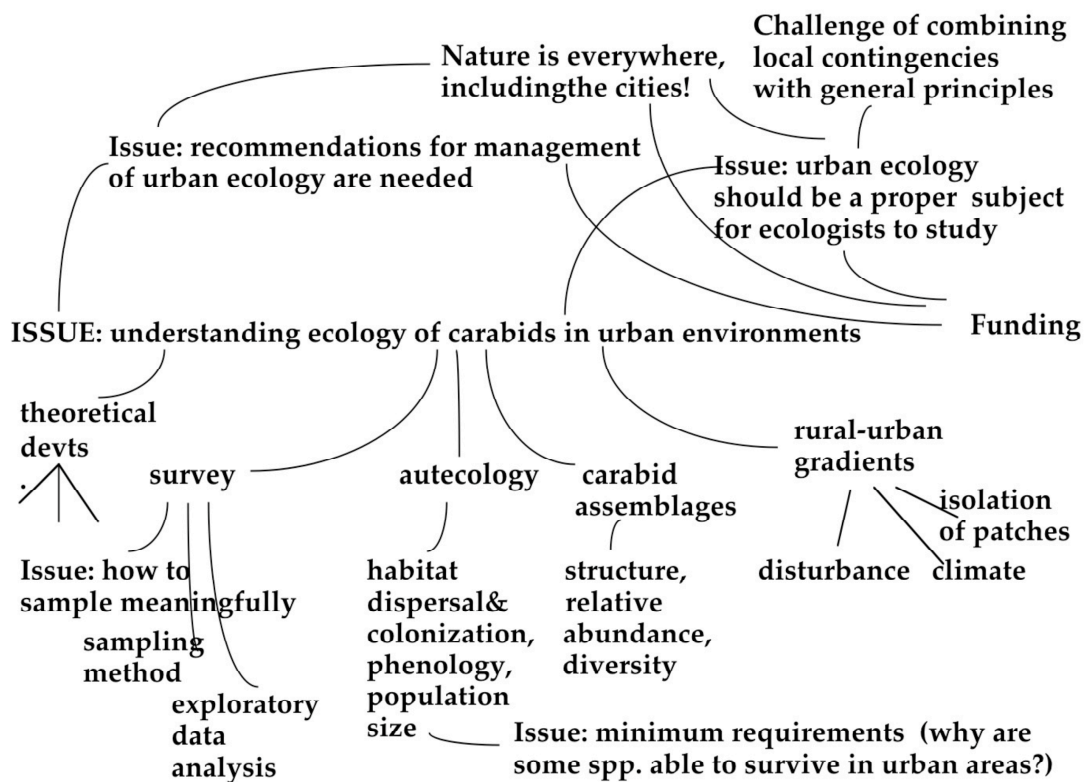


Figure 4. Redrawn outline of a workshop participant's map about how to conduct research on the ecology of carabid beetles in the city of Helsinki (from Taylor 2005, 150)

In this way, a diversity of engagements that might change science can be guided by STS interpretations of the diversity of things scientists do in practice (Taylor 2005, 93ff, 148ff; Clarke 2005; Akera 2007). In practice, mapping opens up "the challenge of bringing into interaction not only a wider range of researchers, but a wider range of social agents, and to the challenge of keeping them working through differences and tensions until plans and practices are developed in which all the participants are invested" (Taylor 2005, 200).

This is a challenge I continue to work on as a teacher and workshop organizer (NewSSC 2010, Taylor and Szteiter 2011, Taylor et al. 2011). However, a different response to the interplay of heterogeneity, control, social infrastructure, and participation runs through this paper. The approach to interpreting scientific projects and influencing their direction centers on "vignettes that opens up questions."

The vignettes are written to communicate to a wide audience that includes scientists, STS scholars, and students. In a pedagogical style, they open up or highlight themes and questions around heterogeneity that have been overlooked or under-emphasized. I have not set out to convince listeners to reject standard accounts and take up alternative concepts, methods, and perspectives. In a spirit of critical thinking, my primary aim has been that listeners see is that they understand things better when they have placed established facts, theories, and practices in tension with alternatives (Taylor 2008). What I expect listeners to do beyond that critical thinking is not addressed with any definiteness or specificity. After all, the questions I raise constitute only one (potential) resource among many in listeners' diverse constructions and reconstructions of knowledge. Perhaps the questions will crystallize for listeners *in their own particular circumstances* an impetus to mobilize different resources and organize them in new directions or, in other words, to build infrastructure for their shaping of society as they establish knowledge.

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