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Atrazine Research and Criteria of Characterizational Adequacy

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Abstract: The effects of atrazine on amphibians has been the subject of much research, requiring the input of many disciplines. Theory reductive accounts of the relationships among scientific disciplines do not seem to characterize well the ways that diverse disciplines interact in the context of addressing such complex scientific problems. "Problem agenda" accounts of localized scientific integrations seem to fare better. However, problem agenda accounts have tended to focus rather narrowly on scientific explanation. Attention to the details of atrazine research reveals that characterization deserves the sort of attention that problem agenda theorists have thus far reserved for explanation.

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1. Background and introduction

Although a consensus has developed around skepticism about the prospects and motivation for Nagelian theory reduction in the biological sciences, several authors have pointed out that participants in this consensus have historically failed to offer much in the way of well-developed alternative philosophical accounts of how various sciences and disciplines might be epistemically related (Rosenberg 1997, Robert 2004); in response to the apparent untenability of theory reduction, proposals of the epistemic relationships among the various biological and allied disciplines have typically been given in terms of explanatory reductionist, anti-reductionist, and nonreductionist (often pluralist) strategies, but a need persists for detailed development of these strategies and application to particular case studies (Brigandt and Love 2012). Contra more radically permissive pluralist accounts (e.g., Dupre 1993), advocates of the so-called "pluralist stance" have contended that the nature of the specific scientific problem or question being addressed constrains the "variety of acceptable classificatory or explanatory schemes." (Kellert et al 2006) Taking onboard this feature of the pluralist stance, Love (2008) and Brigandt (2010) have offered structured accounts of local integrations in evolutionary developmental biology (evo-devo) that are centered around solving particular problems and explaining particular explananda. These local integrations need not, for the authors, necessarily be part of any broader unificatory theoretical reduction of the sort envisioned by proponents of theory reduction (Nagel 1961; Schaffner 1993) or unificatory explanatory ideal (Kitcher 2001). Love and Brigandt's views do, however, emphasis the important role of more problem-specific explanatory (as opposed to theoretical) reductions in biological explanation. Where theory reduction approaches tend to contend that laws describing "lower" mereological levels are always more fundamental in explanation, on the problem-centered view, explanatory fundamentality "*varies with the specific problem* at hand." (Brigandt 2010) Thus, Brigandt and Love's problem-centered integrative frameworks are *nonreductionist* in that they do not necessarily ascribe explanatory fundamentality to lower level epistemic units (laws, theories, models, etc.). However, these frameworks are not *antireductionist* because they reserve a place for reductive explanation when such explanation is called for by the nature of the specific scientific problem or problems under consideration.

Love and Brigandt both take research into *explanations* of evolutionary innovation and novelty as their focus. Hence, Love's and Brigandt's accounts of local integration have centered on questions about multidisciplinary explanation (Love 2008; Brigandt 2010). But while explanation is the *central* concern of many biological projects, explanation is not the *only* concern. Waters (2007) points out that the findings of so-called "exploratory" experiments can have significance for various scientific goals other than explanation and theory development, including knowledge about experimental manipulation and conceptual development to guide future research. Minimally, explanation requires explananda, and those explananda often require scientific investigations to in order to be recognized as things wanting explanation and to disclose the ways in which they might be experimentally manipulated or exploited in the future. Thus, solving scientific problems often requires a certain sort of characterization, achieved through various scientific practices, that is conceptually distinct from explanation. Maps of concentrations of environmental pollutants, for instance, are an outcome of scientific experiments and modeling practices where the goal is experimentally-grounded pattern characterization rather than the provision of an explanatory account of a phenomenon, although the pattern so characterized may later be an object of explanation.

Love (2008) and Brigandt (2010) do not explicitly treat the sort of empirical characterization that I've characterized above (although their projects appear amenable to the inclusion of such a treatment). Love 2008's nonreductionist "problem agenda" account of local (as opposed to more broadly theoretical or unificatory) integration in the biological sciences deploys the concept of "criteria of explanatory adequacy." These criteria, associated with particular problems and sets of problems, act as unifying constraints by specifying what sorts scientific explanations are adequate for the problems that motivate them. I here seek to augment nonreductionist problem-centered epistemologies of multidisciplinary integration with a treatment of the criteria by which various scientific disciplines might judge empirical characterization*s* (as opposed to explanations) and the processes by which such characterizations are generated to be adequate in the context of solving particular problems and sets of problems.

Research into the endocrine disrupting effects of the herbicide, atrazine, is a promising case study because, while concerned with explanation, this research agenda clearly also makes necessary use of empirical characterization (e.g., dose-response curves for atrazine exposure and geographic maps of atrazine concentration). Additionally, atrazine research is remarkably multidisciplinary. Critical evaluation of claims about inherent multidisciplinarity on the part of scientists participating in atrazine research provides an opportunity for describing how certain disciplines play a role in offering answers to the questions that atrazine researchers seek to answer. Articulating the roles played by the contributions of each discipline also presents an opportunity to demonstrate how a nonreductionist epistemology can provide an account of disciplinary integration centered on solving particular problems and answering particular questions. Such an account is desirable not only because it promises to fill the void left by the abandonment of traditional theory reduction approaches for describing epistemic relationships among disciplines, but also because it promises to yield novel insights into reasoning across scientific disciplines and novel interpretations of multidisciplinary disagreement.

2. Atrazine research as a case study

Atrazine is a top selling herbicide that is a persistent and widely distributed ground and surface water pollutant. The effects of atrazine on amphibians and the contribution of these effects to global amphibian decline has been the subject of much research, requiring the input of many disciplines. Work in molecular biology, biochemistry, developmental biology, endocrinology, physiology, and organismal biology has revealed that atrazine acts as an endocrine (hormone) disruptor in vertebrate organisms; it induces a class of enzymes (aromatases) that convert androgens (e.g., testosterone) into estrogens (e.g. estradiol). This conversion has diverse effects on different kinds of vertebrate organisms, from "feminization" leading to decreased reproductive success in frogs to increased cancer rates in humans. Describing and predicting atrazine persistence, transport, and exposure has involved input from diverse disciplines including hydrology, agricultural science, geology, soil science, environmental chemistry, and meteorology (Hayes 2005, Hayes *et al* 2011). Tyrone Hayes, a leading researcher on atrazine's endocrine disrupting effects on frogs, claims that,

> "To truly assess the impact of atrazine on amphibians in the wild, diverse fields of study including endocrinology, developmental biology, molecular biology, cellular biology, ecology, and evolutionary biology need to be invoked. To understand fully the long-term impacts on the environment, meteorology, geology, hydrology, chemistry, statistics, mathematics and other disciplines well outside of biology are required." (2005, 321)

Although understanding physiological developmental mechanisms seems key to understanding abnormal amphibian development resulting from exposure to endocrine disruptors like atrazine, and research on atrazine transport and persistence seems clearly necessary to infer exposure rates and magnitudes, it is not immediately clear what it is about this question that requires input from other disciplines, e.g. evolutionary biology. What justifies Hayes' claim that evolutionary biology is *required*? A framework for structuring multidisciplinary inputs within the atrazine research program can help us articulate the roles played by various disciplines in answering the question of the impact of atrazine's endocrine disrupting effects on amphibians in the wild and thereby allow us to critically evaluate claims (like Hayes's) for the necessity of particular disciplines.

Love (2008) develops an account of localized integration in the sciences based on what he calls "problem agendas," or sets of problems (complex questions composed of simpler questions) related to a particular epistemic goal. Here I cast the impact of atrazine's endocrine disrupting effects on amphibians as a simpler question within the problem (complex question) of the impact of anthropogenic endocrine disruptors on the environment. I will characterize environmental endocrine disruption as a problem shared by the problem agendas of environmental toxicity and developmental endocrine function. To aid in this characterization, I will describe Love's notion of "explanatory adequacy," the criteria by which explanatory answers to problems (complex questions) on a particular problem agenda are judged to be adequate or inadequate. I will then introduce the complementary concept of *criteria of characterizational adequac*y (CCA), criteria by which empirically grounded characterizations and the practices by which they are generated are judged to be adequate or inadequate with respect to particular epistemic goals. I will show how the criteria of characterizational and explanatory adequacy of the two problem agendas of environmental toxicity and developmental endocrine function structure disciplinary inputs with respect to the narrower question of the impact of atrazine's endocrine disrupting effects on amphibians. Finally, I will show how a set of proposed criteria of explanatory and characterizational adequacy drawn from the two problem agendas can make clearer the contributions of evolutionary biology to the question of the impacts of atrazine on amphibians in the wild.

3. Love on local integration

Love (2008) characterizes *problem agendas* as sets of problems (complex questions) related to a particular complex epistemic goal. Problem agendas are united in part by *criteria of explanatory adequacy*, criteria for judging the acceptability of candidate solutions to the problems composing the agenda (875). Against theorists who argue for (typically reductive) stable theoretical integration or unification of diverse fields of science (Nagel 1961; Schaffner 1993), Love argues that integration of multiple fields of study can profitably be localized to particular epistemic goals without necessarily requiring more global theoretical integration or unification.

Criteria of explanatory adequacy are central to Love's account of localized integration. Such criteria make possible "an explicit account of how different areas of research make their contribution without one being more fundamental than another." (2008, 875) Because calls for multidisciplinary research typically arise out of the need to solve problems and answer questions rather than a need for theory-building or testing, what is needed is an account of what ought to count as adequate answers to the complex questions driving the research.

Love uses the problem agenda of evolutionary innovation and novelty as an example to illustrate the concepts of problem agendas and criteria of explanatory adequacy. Problems on the innovation and novelty agenda include, e.g., "How did vertebrate jaws originate?" and "How did avian flight originate?" Although perhaps superficially resembling more ordinary questions (e.g., How was the window broken?) these problems are not standard interrogatives of the sort that can be answered with a single proposition. These problems, due to their complexity and the diversity of simpler questions that they naturally engender, are thought to require multidisciplinary input from developmental, evolutionary, molecular, and systematic biology (2008, 879).

Love claims that the inputs of these disciplines can be structured by the criteria of explanatory adequacy associated with the project. For Love, adequate explanations of the origination of radical evolutionary changes in phenotype must meet three criteria grounded in the nature of the explananda. First, the explanation must address both form and function; e.g., explanations of the origination of vertebrate jaws must include considerations related to how these sorts of jaws function given the particular forms that they take. Second, accounts of origination must explain innovation and novelty at all biological levels of organization as well as relations among these levels, e.g., genetic, cellular, modular, organismal, and population levels (Love 2008, 880). And finally, there is the third criterion of "degree of generalization," which deals with how different problems within the agenda are related. For the case of evolutionary novelty, this criterion can be broken into two further questions. 1- "Can investigations of particular novelties be generalized to other research on different innovations or novelties?" and 2- "Can investigations of model systems be generalized to the phylogenetic juncture relevant to the innovation or novelty under scrutiny?" (Love 2008, 881) The concern here is the appropriateness of generalizations from one problem or question within the agenda to others.

4. The problem of endocrine disruptors in the environment

Environmental problems are exemplary of the sorts of problems that require multi-disciplinary input for generating adequate solutions (Love 2008, 875). The question of atrazine's effects on amphibians in the wild as a result of its endocrine disrupting properties can be viewed as a simpler question located within the environmental problem (complex question) of endocrine disruptors and their ecological impacts. This problem is shared by the problem agendas of environmental toxicity and developmental endocrine function, each with its own criteria of explanatory and characterizational adequacy. These criteria will be shown to constrain and unify attempts at answering questions clustered around the impact of atrazine on amphibians. To illustrate this, I will begin by offering some plausible sample questions germane to the broader question of atrazine's role as an environmental amphibian endocrine disruptor. Notice that the levels of biological organization at which the questions are aimed increases sequentially. The first question is aimed at the biochemical and genetic levels; the second is aimed at the morphological level; the third is aimed at the population level, and the fourth is aimed at global scale ecological phenomena and impacts on higher-level taxa. The species named in the first through the third question are reflective of some of the organisms that are frequently used in such research (Hayes 2005; 2011).

1. What effect does atrazine exposure at a given concentration and duration have on CYP19 (aromatase gene) expression in *Xenopus laevis*?

2. How do the morphological effects of given concentration and duration of atrazine exposure in *Hyperolius argus* differ depending on the developmental stage at which exposure occurs?
3. What impacts do atrazine's endocrine disrupting effect have on *Rana pipiens* populations in Midwestern corn growing regions?
4. Does atrazine's endocrine disrupting effect play a significant role in global amphibian decline?

I want to suggest that answers to these and similar questions will be constrained by criteria of explanatory and characterizational adequacy drawn from the two problem agendas in which problem of environmental endocrine disruption and the question of atrazine's impact on amphibians seem to reside.

5. Environmental toxicity (and a distinction between explanation and empirical characterization)

Environmental toxicology has been described as "the study of the impacts of pollutants on the structure and function of ecological systems." (Landis *et al.* 2010, 1) Its focus is the identification of toxic agents and the establishment of the causal bases of their toxicity (Landis *et al.* 2010, Chapter 3).

These two epistemic goals highlight a distinction between empirical characterization and explanation. In the case of identifying toxic agents, the goal is identifying and characterizing the effects of a chemical and classifying it according to its toxic properties, a task of description and evaluation (characterization). In the case of identifying causal bases of toxicity, the goal is explanatory, concerned with providing a causal account of the processes by which a chemical gives rise to toxic effects. Such explanatory goals seem clearly amenable to constraint by criteria of explanatory adequacy as Love develops the concept. E.g., an explanation of the mechanism by which atrazine is toxic to plants, starvation and harmful oxidative effects due to interruption of plastoquinone-binding in photosystem II (Appleby *et al*. 2001), is constrained by the criterion of explaining higher-level physiological effects by reference to lower-level biochemical processes.

It seems strange, however, to say that the descriptive and evaluative goals of describing and classifying chemicals and their impacts according to toxicity are constrained by *sensu stricto* criteria of *explanatory* adequacy. After all, the goal is description and classification rather than explanation (although as we will see, some descriptive and classificatory claims derive their inferential justification from explanatory accounts). Rather, such attempts at scientific characterization are constrained by what we might call *criteria of characterizational adequacy.* Criteria of characterizational adequacy (CCA) are constraints on empirically grounded characterizations (e.g. claims about response, correlation, concentration, *etc*.) that specify what counts as adequate justification for those sorts of characterizations.

To illustrate how the concept of CCA might apply, consider the case of dose-response curves common to the problem agenda of environmental toxicology. A dose response curve is "a graph describing the response of an enzyme, organism, population, or biological community to a range of concentrations of a xenobiotic." (Landis *et al.* 2010, 36) The task here is characterizational rather than explanatory; such curves have no necessary reference to causal mechanisms explaining the phenomena represented by the graph. However, the production of such a characterization is constrained by certain criteria. For example, the points on the graph must make reference to a concentration of the xenobiotic and must be compared to a control in which the xenobiotic is absent, i.e., the "normal" behavior of the enzyme, organism, population, or biological community under consideration. These "concentration relative" and "compared to control" CCA allow us to see the contributions of exploratory research aimed at characterizing the properties of entities in a way that we could not if we considered only criteria of explanatory adequacy. Much of the research activity in the environmental toxicity problem agenda is aimed at characterizing concentrations (in cells, organs, organisms, particular habitats, *etc.*)(Rohr and McCoy 2010, Hayes *et al*. 2011). Properties of entities at characterized concentrations must then be compared to properties of entities free from the putative toxin, and the characterization of these toxin-free properties involves exploratory research. In the case of atrazine, the near ubiquity of the chemical in fresh water supplies, and its potential for effects at very low doses has necessitated the development of sophisticated filtering techniques and careful attention to laboratory hygiene in order to characterize the properties of biological entities in their atrazine-free conditions. Additionally, due again to atrazine's near ubiquity in the environment, the "compared to control" criterion has made essential early characterizations of frog morphology in the wild (e.g. Witschi 1929), characterizations made before the wide-spread application of atrazine began in the 1950s (Hayes 2004; Rohr and McCoy 2010).

6. Developmental endocrine function

The purpose of the study of developmental endocrine function is to provide an account of the biochemical processes and pathways of hormone synthesis, storage, and physiological function during organismal development (Hayes 2005). Problems (complex questions) comprising a developmental endocrine function problem agenda include “how do sex steroids control development?” and “how do thyroid hormones control development?” Solutions to these sorts of problems would seem to be constrained by the need to address causality at multiple levels of biochemical and biological organization and the need to justify generalizations from insights about pathways and processes in model organisms to claims about other organisms (roughly, Love’s second and third criteria of explanatory adequacy) (Love 2008, 880-881).

Research into sex steroid determination of sexual development provides examples of these criteria in action. Comparative endocrinology research has discovered that androgens and estrogens control sexual development across the vertebrates, although the developmental effects of these hormones vary by taxa, imposing limits on generalizations made across taxa. The effects of these hormones tend to be “organizational” and irreversible at earlier stages of development and “activational” and reversible in adults. Explanations of these effects (and their relative permanence) make reference to biochemical pathways, gene expression, cellular metabolism and differentiation, and organ development (Hayes 2005, Hayes *et al* 2011).

7. Criteria of adequacy applicable the problem of endocrine disruptors in the environment and the narrower atrazine question

Now I wish to show how some of the criteria of explanatory and characterizational adequacy that constrain solutions to problems on the environmental toxicology and developmental endocrinology problem agendas also constrain answering narrower questions germane to assessing atrazine impacts on amphibians. First, because environmental toxicity problem solutions must make reference to controls free from the putative toxin, answers to the question of the impacts of atrazine must be predicated on atrazine exposure effects compared to atrazine-free controls or hypothetical populations. Much of the important research in the "emerging" science of amphibian endocrine disruption has been made possible by basic research on, e.g., CYP19 gene expression, aromatase catalysation of estrogenesis, sex steroid control of sexual differentiation during amphibian development, amphibian reproductive anatomy and behavior, and population genetic modeling of amphibian evolution (2005, Hayes *et al* 2011) Such studies provide a *baseline characterization* against which the effects of atrazine at environmental concentrations inferred by sampling (as well as transport and persistence studies) can be compared. This criterion also provides grounds for the rejection of some proposed answers to questions about atrazine's effects on amphibians. Some authors, for instance, have proposed that hermaphrodism is widespread in wild amphibian populations in the absence of atrazine exposure (Carr and Solomon 2003). However, this conclusion was based on field and laboratory studies in which the controls are thought to have been exposed to environmental atrazine, possible at relatively high concentrations (Hayes 2004; 2005, Rohr and McCoy 2008)

Second, adequate answers to questions about atrazine's effects on amphibians must give an account of all the relevant levels of biological organization. For instance, an answer to the third question in the list above would plausibly give a causal account of the effects of atrazine on Midwestern leopard frog populations by invoking atrazine's role in inducing aromatase expression, enhanced rates of estrogenesis in developing male frogs, demasculization and feminization of affected individuals, decreased reproductive success, and, finally, population level outcomes, e.g. local extinction or adaptation. The absence of this sort of relatively complete mereological level-hierarchical causal chain would imply "black boxes" that would potentially frustrate attempts to explain higher level phenomena in terms of atrazine exposure.

Third, (similar to the third of Love's criteria for explanations of innovation and novelty), adequate answers to questions about atrazine's endocrine disrupting effects on amphibians in the wild must be constrained by considerations of generalization. There seem to be two dimensions of generalization at play here. The first concerns inferring the presence of mechanisms of endocrine disruption (e.g., aromatase induction) in a given clade or clades from the presence of such mechanisms in another clade or clades. The second concerns generalizing from the (biochemical, cellular, organismal, or populational) effects of endocrine disruption in one clade to similar effects in another. With respect to the first dimension, CYP19 aromatase induction due to atrazine exposure seems to be a mechanism conserved across the vertebrate classes, so here generalizations from one amphibian clade to others seem appropriate. Similarly, aromatase catalyzation of estrogenesis appears to be highly conserved (Hayes 2005). With respect to the second dimension, can we infer from population level effects of atrazine in one amphibian clade to similar effects in another? In this case, perhaps not, because sex-steroid mediated developmental endpoints may differ among clades (Hayes 2005), and so population level effects will also be likely to differ.

8. Evolutionary biology

I will now use the above proposed criteria to take up a question that was posed at the outset: what role does evolutionary biology play in research on the ecological effects of atrazine as an amphibian endocrine disruptor? First, evolutionary biology can provide population genetic models of amphibian populations, e.g. models of sex ratios in amphibian clades. These hypothetical populations provide null hypotheses (or baseline characterizations) against which claims of atrazine impact can be tested. This contribution of evolutionary biology is disclosed by consideration of the "compared to control" criterion of characterizational adequacy.

Second, evolutionary and (evolutionary developmental) biology provides models of relations among levels of biological organization. Love says that such relations can be understood spatially and temporally both in ontogeny and evolution. Temporal hierarchies in development articulate the relation of, e.g., gene expression to the formation of physiological pathways and morphological structures (2008, 880). In the atrazine case, developmental endocrinology explains how sex steroids at the biochemical level determine the development of sex-specific traits in amphibians at the organismal level. Evolutionary biology contributes here by providing models linking such traits to population level phenomena; population genetic models can articulate relations between organismal traits and population level effects e.g., covariance between abnormal sex ratios as a result of atrazine-induced feminization (aggregated from the sexual character states of individual organisms) and mean fitness in amphibian clades (Hayes 2010; Guiterres and Teem 2006).

Finally, evolutionary biology contributes phylogenies of relevant traits, e.g. phylogenies of the CYP19 gene, the sex steroids and their receptors, and phylogenies of certain developmental pathways that are mediated by these steroids. Together, these phylogenies are informative about the degree to which atrazine generalizes as an endocrine disruptor and what its likely effects are across diverse amphibian clades. These phylogenies play an important role in satisfying the "generalization" criterion because such phylogenies can either justify or proscribe inferences from research on one clade to claims about another. Importantly for human health, aromatase induction and its effects on sex steroids appear to be conserved across vertebrates (Hayes 2005).

8. Conclusion

Here I've used Love (2008)'s problem agenda framework to characterize research on the impact of atrazine's endocrine disrupting effects on amphibians as addressing a question located within the problem of assessing the impacts of endocrine disruptors in the environment.

This problem is seen as shared by the problem agendas of environmental toxicity and developmental endocrine function. To characterize the epistemic goal of impact assessment central to the environmental problem of endocrine disruptors, I have developed and deployed the concept of criteria of characterizational adequacy, constraints of adequacy on empirically-grounded characterizations and the processes that generate them. This concept, along with Love (2008)'s concept of criteria of explanatory adequacy, make clearer the ways in which various disciplines make their contributions to the problem of atrazine toxicity and the question of atrazine's endocrine disrupting effects on amphibians. In particular, we've seen that evolutionary biology contributes by providing models of relevant evolutionary processes and phylogenies that inform the propriety of generalizing from findings about one clade to claims about others. Evolutionary biology also contributes by providing models of population-level phenomena that may result from organismal-level atrazine exposure effects.

The forgoing treatment of atrazine research can be seen as a further development of Love (2008)'s and Brigandt (2010)'s response to the challenge issued by Rosenberg (1997) and others. This challenge is for those who participate in the skeptical consensus about the prospects and motivation for Nagelian-type theory reduction to provide alternative accounts of the epistemic relations among scientific disciplines. Love and Brigandt have provided nonreductionist accounts of disciplinary integration centered on solving particular problems and providing particular explanations in evo-devo. Here we've seen how Love's problem agenda framework can be applied to another area of research by expanding this framework to include criteria of characterizational adequacy, criteria constraining what counts as an adequate empirically-grounded characterization given the problems that such characterizations are meant to address. In this way, the forgoing treatment of atrazine research is meant to provide a modest contribution the broader project of giving plausible nonreductionist problem-centered philosophical accounts of the epistemic relationships among scientific and especially biological disciplines.

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