The Multilevel Systems Problem of Gene-by-Environment "Interactions"

There is a growing literature on the extent to which individual differences in measures of performance, health, and psychological characteristics (e.g., intelligence) are associated with individuals' genealogical relatedness (e.g., monozygotic vs. dyzogotic twins). Statistical estimates of these associations, often interpreted as the proportion of variance in a characteristic that is explained by genetic differences, are referred to as *heritability estimates* (Bouchard, 2004). These estimates vary widely across characteristics (cf. Bouchard, 2004; Jansen et al., 2015; Polderman et al., 2015) but are often found to be in the 40% to 80% range. Interpretations of the meanings of these associations have been debated from a variety of perspectives (e.g., Manuck & McCaffery, 2014; Plomin et al., 2016; Taylor, 2010; Turkheimer, 2106; Urban et al., 2011), but two interpretations in particular are most concerning to prevention and intervention scientists and practitioners: First is the idea that heritability estimates can inform scientists and practitioners about which characteristics are likely to be most amenable to prevention and intervention efforts; second is the idea that high heritability estimates indicate that genetic influences so determine individuals' characteristics that prevention and intervention efforts are a waste of time, resources, and money. In this paper, I will describe how multilevel systems perspectives bear on these interpretations and conclude that human characteristics are so varied and multiply determined that it is premature to conclude that heritability estimates are a useful means of either (a) identifying viable intervention targets or (b) ruling out any particular targets of prevention or intervention efforts.

Social problems such as crime, poverty, and the social class attainment gap are easy to describe yet difficult to eliminate or prevent. There is a long history of describing the social problems, and possible intervention strategies, in nature and nurture terms, and it is increasingly popular to frame such problems and solutions in terms of gene-by-environment "interactions." From this perspective, prevention and intervention strategies designed to eliminate social problems, such as the social class attainment gap, should be informed by knowledge about both how genes and environments interact and which aspects of those interactions are capable of being modified by the actions of people, communities, or governments.

Although it may be true that knowledge about how genes and environments contribute to social problems can be used to develop effective prevention and intervention strategies, it may also be true that additional knowledge (e.g., about psychological processes) can enable even more efficient prevention and intervention strategies. This possibility raises a number of issues about how best to frame, theoretically and methodologically, questions about social problems and intervention strategies. For example, what does it mean to suggest that (a) environments interact with genes, (b) interactions between genes and environments can be influenced by psychological processes, and (c) genes so determine social problems like the social class attainment gap that prevention and intervention efforts are bound to be ineffective?

If there were a single, modifiable causal factor associated with each social problem, solutions to these problems would be relatively easy to find and implement. However, if we accept the possibility that social problems can be influenced by genes, environments, or their interactions (e.g., Tucker-Drob, Briley, & Harden, 2013), and if we also accept the possibility that the influence of genes, environments, or their interactions can be further influenced by psychological processes (e.g., Slavich and Cole, 2013), then we are confronted with the plausibility that (a) personal and social problems tend to be multiply determined (Cicchetti, 2015; Steg, Buunk, & Rothengatter, 2008) and (b) finding and implementing solutions to these problems will require attending to a diverse range and sequence of causal factors (Cacioppo & Berntson, 1992; Stanovich, 2012). If we add to this set of possibilities the idea that understanding genetic, psychological, or social processes requires specialized disciplinary knowledge (e.g., biology, psychology, sociology) focused on phenomena occurring at fundamentally different *levels of analysis*, then we are in a position to recognize the extent to which the diverse range and sequence of causal factors that multiply determine the creation, maintenance, and resolution of complex social problems constitutes a multilevel systems problem.

In short, the argument I develop here is that, similar to how successful programs for launching spaceships require a detailed understanding of physical systems, successfully implementing prevention and intervention programs that promote healthy personal and community development (e.g., by reducing or eliminating social class attainment gaps) requires a detailed understanding of both (a) biological, psychological, and social systems and (b) the interrelations among the causally-relevant components of these systems. A corollary to this argument is that framing questions about social problems and interventions in terms of either heritability estimates or gene-environment interactions may inadvertently undermine our ability to understand the complexity of the systems that contribute to both social problems and their amelioration via prevention and intervention programs.

Theoretical Issues

Understanding the strengths and limitations of the gene-environment interaction paradigm, and obtaining a detailed understanding of the complexity of social problems and their potential resolutions, will probably require anchoring descriptions of biological, psychological, and social systems to a common, transdisciplinary multilevel systems framework. However, given that a detailed exposition of multilevel systems theories is beyond the scope of this paper (for a summary, see Appendix A), I focus on how the general concepts of *levels of analysis* and *interactions* can both help and hinder our understanding of heritability estimates, gene-environment interactions, and their relevance for prevention and intervention programs designed to alleviate social problems.

Units and levels of analysis. Phenomena that concern social, prevention, and intervention scientists (e.g., crime, poverty, social mobility, health disparities) implicate a wide range of *levels* and *units* of analysis, and the complexity implied by this observation constitutes a multilevel systems problem. The term *units of analysis* is generally used where referring to hypothesized object of measurement; that is, the contents, structures, or processes as reflected to us by our measures (where more reliable and valid measures yield more accurate information about those units). The term *levels of analysis* is generally used where referring to the relations among two or more units of analysis that appear to be qualitatively distinct, or different in kind, as in how cells differ from organs that differ from organisms that differ from organizations.

A vast range of units and "levels" has been studied over the centuries by innumerable scholars who have generally organized themselves into disciplines, institutions, and departments that specialize in understanding a particular set of phenomenon. However, only recently (e.g., the past 7 decades) has the scientific study of *systems* begun to reveal the scope and complex dynamic arrangement of the contents and processes that appear to constitute everything in the universe; which is to say: The levels-of-analysis concept points generally to a very large and complicated set of contents, structures, and processes.

The systematic study of these complex systems has also revealed some common principles (e.g., self-organization, nonlinear dynamics, emergence) that appear to be particularly applicable to understanding living systems (Barton, 1994; Bertalanffy, 1968; Sameroff, 1983; Salthe, 1985, 1993). The levels-of-analysis concept reflects some of these principles, but closer attention to more well-developed multilevel systems theories will almost certainly help us more clearly understand the interrelations among phenomena spread widely across these levels, such as genes, occupational attainment, and social policy. For example, as discussed in Appendix A, where units of analysis are conceived as being materially-nested (e.g., *hierarchically* organized), this nesting imposes constraints on how units can influence each other, or "interact." Notwithstanding the advent of analytic procedures designed to take account of such constraints (e.g., hierarchical linear models), the constraints imposed by such hierarchical organization are rarely discussed by authors who use the term *levels of analysis*, a conclusion that is easily supported by even the most cursory examination of some the more popular levels-of-analysis schemes, termed *psychosocial* (Erikson, 1968), *biopsychosocial* (Engel, 1977), *bioecological* (Bronfenbrenner & Ceci, 1994), *neurons to neighborhoods* (Shonkoff & Phillips, 2000), *molecules to mind* (McEwen, 2001), and *cells to society* (Gehlert et al., 2007). If investigators replaced the vague levels-of-analysis concept with the specific levels-of-organization concept (see Appendix A), they would see immediately that genes do not interact directly with environments; there are many intervening contents and processes required to account for whatever relations they may have in any given case.

This lack of attention to precisely what is meant by any given use of the levels-of-analysis concept probably results largely from the way disciplines tend to be focused on a relatively limited range of units of analysis and in whatever way seems minimally sufficient for understanding and explaining their particular subject matter. This narrow focus, coupled with both a large number of disciplinary specializations and a lack of integration across disciplines, has resulted in many different levels-of-analysis schemes. Accordingly, one way to understand the scope of the multilevel systems problem is to consider the wide range of disciplines focused on describing, predicting, and explaining the phenomena constituting the many possible determinants of personal and social problems (Pellmar & Eisenberg, 2000). A partial list of such disciplines would include sociology, economics, psychology, biology, and chemistry, but a more detailed list would include dozens of increasingly specialized sub-disciples (e.g. molecular biology, social psychology, industrial sociology) and integrative multi-disciplinary fields (e.g., computational epidemiology, social neuroscience, public health).

For any given line of inquiry, the relevant units of analysis may exist on only one level but generally implicate three or more levels. For example , whether we define healthy personal development in biological (e.g., diabetes), psychological (e.g., depression), or social (e.g., occupational attainment) terms – or healthy social development in economic (e.g., income disparities), sociological (e.g., social class inequalities), or epidemiological (e.g., unemployment rates) terms – each definition can be framed in terms of a particular focal level of analysis yet invariably implicates a wide range of additional levels of analysis (Anderson, 1998; Kaplan, Everson, & Lynch, 2000; Mathieu & Chen, 2011). Similarly, where focusing on social problems such as the social class attainment gap or stagnant social mobility – particularly intergenerational social mobility defined generally as individuals increasing their economic, educational, or occupational status relative to their family of origin – we will usually benefit from taking account of biological (e.g., genetic), psychological (e.g., motivation), and social (e.g., labour market) factors, and these factors can be viewed as existing within, and interacting functionally across, an even wider range of levels of analysis (Anderson, 1998, 1999; Mezuk et al., 2013; Thienpont & Verleye, 2004).

If we accept that molecular (e.g., genetic), organismic (e.g., human), and population (e.g., nation) phenomena occur at different levels of analysis, then questions about gene-environment "interactions" and their relations to developing individuals and communities necessarily implicate many additional potentially-intervening units and levels of analysis. Whether or not, and to what extent, these additional units and levels of analysis are causally relevant to the problem being studied are theoretical and empirical questions that have barely begun to be addressed. However, from a multilevel systems perspective, we have good reasons to believe that theoretical and analytic models focused on complex social problems implicating widely disparate units and levels of analysis will benefit from a more systematic understanding of the potentials and constraints characterizing multilevel systems (see Appendix A). In short, complex questions about things like: the implications of heritability for early intervention, social mobility, and the social class attainment gap (and their potential intergenerational transmission) should be viewed as multilevel systems problems requiring multilevel theoretical, methodological, and practical solutions. Consequently, developing coherent and effective theoretical, methodological, and practical strategies for understanding the nature of, and relations among, causal factors related to social problems and their solutions will likely be hastened by at least a rudimentary understanding, and probably a detailed understanding, of multilevel systems.

Jingle and jangle fallacies. Attendant to these many levels of analysis and disciplinary specializations is a burgeoning lexical morass, in which the same terms are used where referring to different phenomena (i.e., jingle fallacies) and different terms are used where referring to the same phenomena (i.e., jangle fallacies). For example, using the same term (e.g., interaction) where referring to different things (e.g., statistical relations and causal dynamics) is a jingle fallacy, and using different terms (e.g., biological organism, psychological system, social agent) where describing the same thing (e.g., a person) is a jangle fallacy. Pedhazur and Schmelkin (1991) illustrated the undermining effects these fallacies can have on clear thinking and communication by arguing, further, that "the jingle fallacy refers to the belief that, *because* different things are called by the same name, they are the same thing. Conversely, the jangle fallacy refers to the belief that things are different from each other, *because* they are called by different names" (p. 74). Together, jingle and jangle fallacies inevitably undermine the development of consensual nomenclature and common frames of reference that might otherwise hasten the kind of clear understanding, productive communication, and cumulative scientific knowledge that would enable the most efficient prevention and intervention efforts (Block, 1995; Hernandez & Blazer, 2006; Wimsatt, 2013).

Given the complexity implied by levels-of-analysis schemes and the confusion engendered and perpetuated by rampant jingle and jangle fallacies, rigorously addressing questions about complex social problems and their prevention or remediation will likely require avoiding approaches that are framed only in terms of a few possible causal factors associated with a few vaguely articulated levels of analysis – such as intra-individual (e.g., molecular), individual (i.e., organismic), or extra-individual (e.g., population) factors, or even two of these presumed factors (e.g., genes and environments) – and cultivating approaches capable of defining and interrelating simultaneously all relevant factors within a common frame of reference. As discussed below, this does not mean that we have to take account of all relevant factors at the same time; it just means that a common framework should be able to take them into account when necessary.

In the absence of a common framework, we have no way of knowing, for example, what units and levels are likely to necessary to account for where considering how genes and environment influence each other. We also have no way of knowing the extent to which any given levels-of-analysis scheme maps on to any other levels-of-analysis scheme, which it makes it difficult to determine the extent to which diverse accounts of such intervening units and levels are related to each other. In other words, using the bare term *levels of analysis* as if everyone knows and agrees on what it means is confusing and perpetuates a jingle fallacy by making it sound like two people are talking about the same thing when, in fact, they may be talking about two very different things, thereby undermining our ability to generate cumulative scientific and practical knowledge.

There are innumerable instances of this kind of confusion and its consequences, particularly where addressing questions about the extent to which "nature" and "nurture" factors are relevant for understanding a particular phenomenon. For example, where describing ongoing controversies about the extent to which observed behaviors were due more to nature or nurture, Sherman (1988) argued that "after two decades of unenlightening debate, it became apparent to Mayr (1961), Tinbergen (1963) and Lehrman (1970) that the lack of consensus was mainly due to semantic and conceptual issues, rather than to discrepancies of fact" (p. 616). Similarly, Taylor (2015) argued:

> In the long history of nature-nurture debates, opposing sides often assume, imply, or propose that these different sciences are speaking to the same issues. This sense of equivalence or, at least, mutual relevance is evident most notably in discussions that create or play on ambiguity in the meaning of the technical term heritability as well as in unwarranted interpretation of other

fractions of variation in terms of differences in yet-to-be identified environmental factors" (Taylor, 2015, p. 75)

From a multilevel systems perspective, these kinds of conceptual issues are practically inevitable because we have no common framework for agreeing on what we mean by levels of analysis or on how the concept of levels of analysis may differ from what may appear to be similar concepts, such as *levels of description* or *levels of organization* (described below).

However, if we were to replace the general concept of levels of analysis with the more specific concepts of levels of description (e.g., describing things using different levels of abstraction) and levels of organization (e.g., describing things as existing at different materially-nested levels of hierarchical organization), we would be in a better position to appreciate the kinds of confusion that can result where failing distinguish between *how we describe things* and *the things we are describing*. For example, we can say that a person exists at a level of organization above organs and below social groups. This "person level" of organization does not change as a function of the point of view from which it is observed and can be clearly understood as one of three different levels of organization.

Using levels of description, however, can obscure such clear distinctions between levels of organization. For example, describing a person from different disciplinary perspectives (e.g., as a "biological organism," a "psychological system," or a "social agent"), without explicit reference to levels of organization, tends to promote both jangle fallacies (e.g., by using different terms [i.e., biological, psychological, social] to refer to the same thing [i.e., person]) and jingle fallacies (by using the term person to mean more than one thing [e.g., cells, tissues, organs; thoughts, feelings, behaviors; and daughter, student, citizen]). Obviously, there is "truth" related to each of these descriptions (and these descriptions can be usefully applied), but using such descriptions without reference to an objective system of levels (e.g., levels of organization) results in a seemingly endless array of descriptive systems (hence terminological confusion at the expense of theoretical integration). Given that there is a practically infinite range of descriptions that can be applied to any given phenomenon, we can sharpen our understanding of levels of analysis by focusing more on levels of organization (and other more well-specified multilevel systems; see Appendix A) and avoiding, as far as reasonably possible, the excessive variety of descriptions that fill more book and journal pages than any human could possibly read and reconcile.

Finally, despite its inherent vagueness (see Appendix A), the generic levels-of-analysis approach has probably played an historically-important role in advancing multilevel systems science because it helps us avoid a particularly vexing type of jingle fallacy: *unitary fallacies*; "that is, treating things occurring at different levels of a multilevel system as if they exist and function at a single level" (Peck, 2007, p. 1129). Many people are probably familiar with this kind of problem by way of the analytic and inferential challenges associated with analyzing nested data and interpreting the results (e.g., using hierarchical linear modeling to account for dependencies due to nesting and avoiding the *ecological fallacy* of interpreting group-level relations as if they apply equally to individual-level relations) (Bryk & Raudenbush, 1992, Klein & Kozlowski, 2000). However, regardless of its historic importance, the inherent vagueness of generic levels-of-analysis approaches suggests that a more formal approach to multilevel systems will be necessary for describing and interrelating systematically the many components that multiply-determine phenomena such as social class attainment and mobility. Using these more well-defined multilevel systems frameworks will also likely afford significantly more interdisciplinary integrative potential (e.g., consensual nomenclature that has consistent meaning across a wide range of disciplines) that will, in turn, allow for clear communication and more efficient prevention and intervention efforts.

Methodological Issues

Given the extent to which analytic models are informed by theoretical models, coupled with either the vague use of levels-of-analysis schemes or the complete neglect of multilevel systems, dominant analytic approaches (e.g., analysis of variance and regression analysis) tend to be based on either single-level or unidimensional theoretical models. Further, reflecting concerns that "theoretical thinking is shackled by the methodology of the day" (Bergman, 1992, p. 147), even where some kind of levels-of-analysis scheme is implicit in the theoretical model, investigators regularly treat their data as if they conformed to a single-level theoretical model. For example, standard general linear modeling (GLM) approaches to data analysis, such as those generally used to generate heritability estimates, assume that units of analysis (a) exist and function on the same "level," (b) are relatively homogeneous, and (c) interact linearly (e.g., Bar-Yam, 2002; Holland, 1995; Magnusson & Stattin, 1998; Richters, 1997; von Eye & Bergman, 2003).

From a multilevel systems perspective, none of these assumptions is likely to be true, particularly where studying complex social problems and intervention programs believed to be influenced by genes, environments, gene-environment interactions, and other factors (e.g., subjective perceptions). For example, the range of factors that multiply determine things like social mobility and social class attainment almost certainly (a) exist on multiple levels; (b) cohere heterogeneously within individuals and social contexts; and (c) interact nonlinearly both within and across many levels of analysis. In addition to GLMs being based on unrealistic assumptions, their ability to incorporate the full range of implicated units and levels of analysis in multiply-determined systems makes them susceptible to *third variable* problems, or model misspecification. Consequently, regardless of how well an analyst incorporates the additive or multiplicative forms of statistical interaction into their model, it strains credulity to suppose that the results of GLM analyses are capable of revealing much accurate or useful information about any hypothesized causal dynamics linking genetic, environmental, psychological, and attainment factors.

Popular extensions of standard GLMs (e.g., random-coefficient models) have been designed to address "multilevel" issues (e.g., Berntson & Cacioppo, 2006; Bremner, 2006; Bryk & Raudenbush, 1992; Diez-Roux, 1998; Hawkley et al., 2007; Holmes et al., 2008; Hox & Stoel, 2005; Kaplan et al., 2000; Klein & Kozlowski, 2000; Luke, 2004) yet tend to be based on narrow conceptualizations of multilevel systems (e.g., hierarchically-nested levels of aggregation) that pertain only partially to the full spectrum of multilevel systems that pervade the natural world (see Appendix A). Cross-classified random effects models (e.g., Luo & Kwok, 2009; Meyers & Beretvas, 2006) use a broader concept of multilevel systems but appear to be of similarly limited use for handling the extent of complexity implicated by nonlinear causal dynamics flowing through a large number of intertwined hierarchically- and heterarchically-nested multilevel systems (see Appendix A).

More closely aligning analytic with theoretical models requires developing and using more versatile measurement, statistical, mathematical, and simulation modeling approaches (cf. Bosse et al., 2007, 2009; Brown et al., 2014; Diez-Roux, 2007; Holland, 2006; Holmes et al., 2008; Kasabov et al., 2008; Kohl et al., 2000; Magnusson, 1985, 2003; Mathieu & Chen, 2011; Molenaar, 2004; Roco & Bainbridge, 2002; Thakar et al., 2007; Urban, Osgood, & Mabry, 2011; Voit, Qi, & Miller, 2008); such as, pattern-centered, computational, agent-based, hybrid computational-agent, and other mathematical and simulation models capable of better reflecting the complex systems being studied. In addition to reflecting more realistically the complexity of the phenomena being studied, simulation models in particular are a powerful means for examining situations that may not be realized in any given data set (Diez-Roux, 2007; Lich et al., 2013). For example, given a fairly well-specified simulation model that includes information about genetic, psychological, attainment, community, and policy factors, analysts could explore the implications (e.g., costs and consequences) of different policy decisions or intervention strategies before spending significantly more time, energy, and money on conventional methods (e.g., collecting data from large samples) for evaluating such decisions or strategies.

The concept of *interaction* is especially problematic. The popular and scientific literature refers often to the concept of gene-environment interactions, but the meaning of the term interaction deserves more careful consideration. Given the central role played by the concept of interaction in discussion of gene-environment interaction, it would be helpful to assume that we were all using the same definition of interaction. However, there are a lot of different things that can be meant by the term interaction (Phillips, 2008; Taylor, 2015; VanderWeele, 2012). In addition to the many different ways interaction models can be constructed statistically (Manuck & McCaffery, 2014), such as additive or multiplicative interaction models, critical distinctions between statistical and other forms of interaction (e.g., mechanistic) are too often overlooked.

Given that moving from research results to practical interventions involves moving from statistical abstraction to actual physical contact, it becomes practically imperative to distinguish statistical interactions from other forms of interaction (e.g., mechanistic and functional interactions) (Phillips, 2008; VanderWeele, 2012). At the very least, using a more precise and explicitly defined concept of interaction will help avoid construing statistical correlations as evidence of causal relations and provide a more specialized language for describing causal relations among system components. In other words, distinguishing explicitly between statistical and mechanical or functional interactions encourages descriptions of gene-environment relations that distinguish between correlations among components (e.g., proportion of variance) and the hypothesized causal dynamics among components.

Distinguishing between statistical and mechanical or functional interactions also encourages replacing GLM approaches with models that are more ideally suited for representing complex, nonlinear, dynamic systems (e.g., connectionist, agent-based, and hybrid simulations as well as other pattern-centered approaches). For example, as Diez-Roux (2007) argued:

> Although different models for the integration of social and biologic factors may be useful in specific circumstances, the most general (and probably the most ‘‘realistic’’) views social and biologic factors as tightly entwined in complex systems. The social antecedents model and the gene-environment interaction model are in fact reduced cases of this more general model. (p. 571)

These more nuanced models better incorporate what we know about complex social problems and allow us to evaluate more easily the probable implications of making changes to any particular component within the overall system (Auffray & Nottale, 2008; Diex-Roux, 2007; Noble, 2012; Parker & Srivastava, 2013). In short, inferring that social mobility or the social class attainment gap is, or can be, influenced by genes, environments, or gene-environment interactions on the basis of almost any conventional (e.g., GLM) statistical analysis is a dubious practice because estimates of statistical interactions are generally an insufficient basis for making inferences about the substantive (e.g., mechanical or functional) interactions reflecting the nonlinear dynamic processes likely to influence such mobility or gaps.

Practical Issues

Prevention and interventions efforts are ideally designed on the basis strong theoretical and empirical models. Given few well-developed multilevel systems theories and models, we have probably yet to see the most well-developed prevention and intervention programs implicated by the large volume of relevant, but yet to be sufficiently integrated, evidence. Nevertheless, this patchwork of theory and evidence does provide a lot of useful knowledge. From a multilevel systems theory perspective, one of the most important themes running through this knowledge base is the idea that the most successful prevention and intervention efforts will be those that target simultaneously units of analysis at several levels of the overall person-in-context system (Chinman et al., 2008; Cichetti, 2015; Diez-Roux, 2007; Dodge et al., 2008, 2015; Greenberg et al., 2003; Hernandez & Blazer, 2006; Huang et al., 2009; Johnson et al., 2010; Rydin et al., 2012; Schomerich & Kawachi, 2016; Schulz et al., 2011; Stanovich, 2012; Trickett & Beehler, 2013; Trochim et al., 2006; Weeks et al., 2103).

This conclusion follows most directly from evidence indicating that variations among units on any particular level of analysis (e.g., genes, behavior, community resources) are multiply determined by units from a diverse range of additional levels of analysis (see Appendix A). In these terms, targeting prevention and intervention efforts on a single unit from a single level of analysis is likely to result in weak effects because the effects of changing that unit will likely depend on the effects of other units (e.g., nonlinear dynamic interactions). For example, Dodge et al. (2008) described a “dynamic cascade” (p. 1910) model of adolescent violence involving 7 causally relevant and interdependent factors, ranging from being born into an “adverse social context, characterized by high neighborhood disadvantage and low neighborhood access to social services” (p. 1910) to socializing with deviant peers into adolescence. In this model, factors from diverse levels of analysis (which, in this case, did not include specific reference to whatever genetic factors may also play roles in the development of impulsive or violent behavior), converge cumulatively and nonlinearly on developing individuals to increase or decrease the probability of engaging in violent behavior. The dynamic cascade model highlights both the role of multiply-determining processes and the many places within the system where interventions could be targeted.

Importantly, whereas cumulative risk models based on summing across a set of dichotomized risk factors can successfully predict relevant outcomes (Sameroff et al., 2003), they contribute little to explaining those outcomes. Where explanations are necessary, we need more detailed information about the actual interfaces among the various parts of the person-in-context system, where the real action of interventions occur. Studies that take a gene-environment interaction approach, or that otherwise consider the extent to which any given outcome is multiply determined, move us closer to the kind of detailed information likely to be most helpful for designing effective interventions.

For example, studies of wealth transfer from lower to higher social classes have generally focused on single variables but suggest roles played by several factors; such as, technology, immigration of unskilled workers, outsourcing, and labor unions (Stanovich, 2012). To the extent that there are interactions among these factors (e.g., weak labor unions result in more outsourcing that results in more technology use that depends on skilled workers), focusing prevention or interventions efforts on only one of these factors is likely to produce limited effects on wealth transfer. Similarly, evidence that learning disabilities influence social class attainment suggests intervening on learning disabilities; however, because variations in learning disabilities have also been associated with several biological (e.g., genetic) and social (e.g., instructional and home quality) factors, the most effective prevention and intervention efforts will likely result from focusing simultaneously on genetic and social factors. For example, genetic data may suggest particular strengths and weaknesses with respect to particular social environments for particular subgroups of individuals; in such cases, different prevention and intervention strategies may need to be tailored to these different subgroups.

These relatively general approaches can probably provide useful information, but approaches that focus more specifically on the real action of intervention will likely generate even more useful information. For example, the real action of intervention can be viewed as the transaction between targets of intervention (e.g., individual, family, service center) and the policy or organizational system that provides the intervention. Between these targets and systems, which can be viewed as existing and function at two different focal 'levels of analysis,' there are typically several intervening levels of analysis. Optimally implemented interventions will be those that closely attend to how units of analysis patterned at the "highest" level interface with those patterned at the next "lower" level (e.g., training staff), and then to how those lower-level units interface with the next lower level units (e.g., service center managers), and so on to the intended target, such as the front-line staff or their clients. Conceived in this way, the effects of policy-level intervention decisions on the intended intervention targets must cascade through intermediary systems. Consequently, their effectiveness can be expected to vary in proportion to how well their designs, strategies, and implementation features incorporate relevant information about inter-unit relevance (e.g., designed based on an accurate theory of change) and inter-level fit (e.g., the combined effects of design and implementation fidelity).

As Shonkoff (2010) argued, "the question is not whether decisions about the allocation of resources should be informed by evidence, but whether the current definition of evidence that guides early childhood investments may be too narrow" (p. 362). Observational studies, examination of gene-environment interaction models, randomized control trials, and cost-benefit analyses yield a wide range of useful information, but they may not promote the kind of integrative and innovative thinking necessary to design the most effective prevention and intervention programs. For integrative and innovative thinking inspiration, we can look to developmental and systems science approaches that focus more explicitly on the extent to which successful development is multiply determined by a wide range of factors (Ciccheti, 2015; Belsky & Pluess, 2009; Shonkoff, 2010). For example, it is probably not enough to know that early experiences influence epigenetic processes; the most effective intervention efforts will likely come from knowing more about the details of such dynamic process, such as how social and epigenetic processes interact with the specific social, emotional, and cognitive skills that promote choices and behavior associated with positive development (Shonkoff, 2010).

In short, from a multilevel systems perspective, the reason that explaining is so much more important than predicting is that theories and models focused on explaining are more likely to reveal the kind of details necessary for effective intervention. Shifting attention from the abstractions of prediction and statistical interaction to the mechanistic and functional interactions characterizing the real action of prevention and intervention efforts is likely to reveal a set of more specific contents, structures, and dynamic processes occurring within and between units of analysis situated at the interface between adjacent levels of analysis. This detailed information about the interface between units of analysis at adjacent levels of analysis within the dynamic cascade of developing person-in-context systems should provide relatively clear information about where, when, and how to focus prevention and intervention efforts. In these terms, as discussed previously, results from heritability studies tell us very little, or perhaps nothing, about these critically important causal dynamics that pervade person-in-context systems.

Conclusions

This brief summary of how multilevel system theory perspectives bear on the relevance of heritability estimates and gene-environment interaction studies for designing and implementing prevention and intervention efforts yields several conclusions. First, acquiring a detailed understanding of multiply-determined personal and social problems and their potential resolutions will almost certainly require anchoring descriptions of biological, psychological, and social systems to a common, transdisciplinary multilevel systems framework. In addition to enabling interdisciplinary integration (e.g., clear communication about consensually agreed upon phenomena), using well-defined multilevel systems frameworks should also highlight specific details of the dynamic interface between units of analysis at adjacent levels of analysis.

Second, more closely aligning analytic with theoretical models by restricting the use of GLM approaches to narrowly defined problems that conform to the attendant assumptions; developing and using measurement, statistical, mathematical, and simulation modeling approaches that are sensitive to multilevel nonlinear dynamics; and distinguishing explicitly and consistently between statistical and mechanistic or functional forms of interaction should generate significantly more actionable evidence that better reflects the complex systems being studied. Third, moving from theory and research to practical interventions involves moving from vague approaches to the levels-of-analysis concept and statistical abstractions to actual mechanistic (e.g., physical) and functional (e.g., psychological meaning) contact between practitioners and clients. Given that units of analysis on any particular level of analysis are multiply determined by units of analysis from a diverse range of additional levels of analysis, approaches that focus more specifically on the real action of intervention, at the interface of adjacent levels of analysis, will likely generate the most useful information for designing and implementing prevention and intervention strategies.

In short, from a multilevel systems theory perspective, given that personal and social problems are so varied and multiply determined, GLM approaches so inappropriate for modeling heterogeneous nonlinear dynamic systems, and heritability estimates so theoretically and methodologically disconnected from the dynamic processes that generate human characteristics: The ideas that heritability estimates can inform scientists and practitioners about which characteristics are likely to be most amenable to prevention and intervention efforts or that high heritability estimates reveal anything in particular about genetic influences, least of which that genes completely determine traits or behavior, can be seriously questioned if not completely rejected.

References

Ahl V., & Allen, T. F. H. (1996). *Hierarchy theory: A vision, vocabulary, and epistemology.* New York: Columbia.

Anderson, N. B. (1998). Levels of analysis in health science: A framework for integrating sociobehavioral and biomedical research. *Annals of the New York Academy of Sciences, 840,* 563-576.

Anderson, N. B. (1999). Solving the puzzle of socioeconomic status and health: The need for integrated multilevel, interdisciplinary research. In N. E. Adler, M. Marmot, B. S. McEwen, & J. Stewart (Eds.), *Socioeconomic status and health in industrial nations: Social, psychological, and biological pathways* (pp. 302-312). New York: New York Academy of Sciences.

Aronson, L. R. (1987). Some remarks on integrative levels. In G. Greenberg, & E. Tobach (Eds.), *Cognition, language, and consciousness: Integrative levels* (pp. 269-276). Hillsdale, NJ: Erlbaum.

Auffray, C. & Nottale, L. (2008). Scale relativity theory and integrative systems biology: 1 Founding principles and scale laws. *Progress in Biophysics and Molecular Biology, 97*, 79–114.

Barton, S. (1994). Chaos, self-organization, and psychology. *American Psychologist, 49*, 5-14.

Bar-Yam, Y. (2002). Unifying principles in complex systems. In M. C. Roco & W. S. Bainbridge (Eds.), Converging technologies for improving human performance: Nanotechnology, Biotechnology, Information Technology, and Cognitive Science (NBIC) (pp. 380-409). NSF/DOC-sponsored report. http://www.wtec.org

Belsky, J., & Pluess, M. (2009). Beyond diathesis stress: Differential susceptibility to environmental influences. *Psychological Bulletin*, *135*(6), 885-908.

Bergman, L. R. (1992). Studying change in variables and profiles: Some methodological considerations. In J. B. Asendorpf & J. Valsiner (Eds.), *Stability and change in development: A study of methodological reasoning* (pp. 143-149). Newbury Park: Sage.

Berntson, G. G., & Cacioppo, J. T. (2003). A contemporary perspective on multilevel analyses and social neuroscience. In F. Kessel, P. L. Rosenfeld, & N. B. Anderson (Eds.), *Expanding the boundaries of health and social science: Case studies in interdisciplinary innovation* (pp. 18-40). New York: Oxford University Press.

Berntson, G. G., & Cacioppo, J. T. (2006). Multilevel analysis: Physiological and biochemical measures. In M. Eid & E. Diener (Eds.), *Handbook of multimethod measurement in psychology (pp. 157-172)*. Washington, DC: American Psychological Association.

Berntson, G. G., & Cacioppo, J. T. (2008). The neuroevolution of motivation. In J. Shah & W. Gardner (Eds.), *Handbook of motivation science* (pp. 188-200). New York: Guilford

Bertalanffy, L. von (1968). *General system theory: Foundations, development, and applications* (revised edition). New York: Braziller.

Block, J. (1995). A contrarian view of the five-factor approach to personality description. *Psychological Bulletin, 117,* 187-215.

Bosse, R., Jonker, C.M., & Treur, J. (2007). Simulation and analysis of adaptive agents: An integrative modeling approach. *Advances in Complex Systems*, *10*(3), 335-357.

Bosse, T., Gerritsen, C., & Treur, J. (2009). Towards integration of biological, psychological and social aspects in agent-based simulation of violent offenders. *Simulation*, *85,* 635-660.

Bouchard, T. J. (2004). Genetic influence on human psychological traits: A Survey. *Current Directions In Psychological Science*, *13*(4), 148-151.

Bremner, J. D. (2006). Traumatic stress from a multiple-levels-of-analysis perspective. In D. Cicchetti & D.J. Cohen (Eds.), *Developmental Psychopathology* (2nd ed., pp. 656-676). Hoboken, NJ: Wiley.

Bronfenbrenner, U., & Ceci, S. J. (1994). Nature-nuture reconceptualized in developmental perspective: A bioecological model. *Psychological Review*, *101*(4), 568-586.

Bronson, G. (1965). The hierarchical organization of the central nervous system: Implications for learning processes and critical periods in early development. *Behavioral Science, 10*, 7-25.

Brown Urban, J., Osgood, N., Okamoto, J., Mabry, P., & Hassmillier Lich, K. (2014). Developmental systems science: Extending developmental science with systems science methodologies. In P. M. Molenaar, R. M. Lerner, K. M. Newell, P. M. Molenaar, R. M. Lerner, K. M. Newell (Eds.) , *Handbook of developmental systems theory and methodology* (pp. 95-127). New York, NY, US: Guilford Press.

Bruni, L. E., & Giorgi, F. (2015). Towards a heterarchical approach to biology and cognition. *Progress in Biophysics and Molecular Biology, 119*, 481-492.

Bryk, A., & Raudenbush, S. (1992). *Hierarchical linear models in social and behavioral research: Applications and data analysis methods.* Newbury Park: Sage Publications.

Cacioppo, J. T., & Berntson, G. G. (1992). Social psychological contributions to the decade of the brain: Doctrine of multilevel analysis. *American Psychologist, 47,* 1019-1028.

Campbell, D. T. (1990). Levels of organization, downward causation, and the selection-theory approach to evolutionary epistemology. In G. Greenberg, & E. Tobach (Eds.), *Theories of the evolution of knowing* (pp. 1-17). Hillsdale, NJ: Erlbaum.

Chinman, M., Hunter, S. B., Ebener, P., Paddock, S. M., Stillman, L., Imm, P., & Wandersman, A. (2008). The getting to outcomes demonstration and evaluation: An illustration of the prevention support system. *American Journal of Community Psychology*, *41*(3-4), 206-224.

Cicchetti, D. (2015). Preventive intervention efficacy, development, and neural plasticity. *Journal of the American Academy of Child & Adolescent Psychiatry*, *54*(2), 83-85

Crumley, C. L. (1995). Heterarchy and the analysis of complex societies. *Archeological Papers of the American Anthropological Association, 6*(1), 1-5.

Crumley, C. L. (2015). Heterarchy. In R. Scott & S. Kosslyn (Eds.), Emerging Trends in the Social and Behavioral Sciences: An Interdisciplinary, Searchable, and Linkable Resource, 1-14.

Derryberry, D., & Tucker, D. M. (1991). The adaptive base of the neural hierarchy: Elementary motivational controls on network function. In R. A. Dienstbier (Ed.), *Nebraska symposium on motivation* (Vol. 38, pp. 289-342). Lincoln: University of Nebraska Press.

Diez Roux, A. V. (1998) Bringing context back into epidemiology: Variables and fallacies in multilevel analysis. *American Journal of Public Health, 88,* 216-222.

Diez Roux, A. V. (2007). Integrating social and biologic factors in health research: A systems view. *Integrating Social and Biological Factors*, *17*(7), 569-574.

Dodge, K. A., Greenberg, M. T., & Malone, P. S. (2008). Testing an idealized dynamic cascade model of the development of serious violence in adolescence. *Child Development*, *79*(6), 1907-1927.

Dodge, K. A., Bierman, K. L., Coie, J. D., Greenberg, M. T., Lochman, J. E., McMahon, R. J., & Pinderhughes, E. E. (2015). Impact of early intervention on psychopathology, crime, and well-being at age 25. *The American Journal Of Psychiatry*, *172*(1), 59-70.

Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. *Science*, *196*, 129-136.

Erikson, E. H. (1968). *Identity: Youth and crisis.* New York: Norton.

Gehlert, S. (2008, April). *Multi-level approaches to targeting health disparities in the United States.* Paper presented at the meeting of the 20th National Symposium on Doctoral Research in Social Work, Columbus, OH.

Greenberg, M. T., Weissberg, R. P., O'Brien, M. U., Zins, J. E., Fredericks, L., Resnik, H., & Elias, M. J. (2003). Enhancing school-based prevention and youth development through coordinated social, emotional, and academic learning. *American Psychologist*, *58*(6-7), 466-474.

Grene, M. (1988). Hierarchies and behavior. In G. Greenberg, & E. Tobach (Eds.), *Evolution of social behavior and integrative levels* (pp. 3-17). Hillsdale, NJ: Erlbaum.

Hawkley, L. C., Preacher, K. J., & Cacioppo, J. T. (2007). Multilevel modeling of social interactions and mood in lonely and socially connected individuals: The MacArthur social neuroscience studies. In A. D. Ong & M. van Dulmen (Eds.), *Oxford Handbook of Methods in Positive Psychology* (pp. 559-575). New York: Oxford University Press.

Hernandez, L. M., & Blazer, D. G. (Eds.) (2006). *Genes, behavior, and the social environment: Moving beyond the nature/nurture debate.* Committee on Assessing Interactions Among Social, Behavioral, and Genetic Factors in Health, Institute of Medicine. Washington, DC: National Academy Press.

Herrick, C. J. (1949). A biological survey of integrative levels. In R. W. Sellars, V. J. McGill, & M. Farber, *The quest of modern materialism* (pp. 222-242). New York: MacMillan.

Holland, J. H. (1995). *Hidden order: How adaptation builds complexity.* New York: Addison-Wesley.

Holland, J. H. (2006). Studying complex adaptive systems. *Journal of Systems Science & Complexity, 19*, 1-8.

Holmes, J. H., Lehman, A., Hade, E., Ferketich, A, K., Gehlert, S., Rauscher, G. H., et al. (2008). Challenges for multilevel health disparities research in a transdisciplinary environment. *American Journal of Preventative Medicine, 35(2S)*: S182-S192.

Hox, J. J. & Stoel, R. D. (2005). Multilevel and SEM approaches to growth curve modeling. In B. S. Everitt & D. C. Howell (Eds.), *Encyclopedia of Statistics in Behavioral Science* (pp. 1296-1305). Chicester, UK: Wiley.

Huang, T. T,, Drewnowski, A., Kumanyika, S. K., & Glass T. A. (2009). A systems-oriented multilevel framework for addressing obesity in the 21st century. *Preventing Chronic Disease, 6*(3), 1-10. http://www.cdc.gov/pcd/issues/2009/jul/09_0013.htm. Accessed July 23, 2015.

Jansen, A. G., Mous, S. E., White, T., Posthuma, D., & Polderman, T. C. (2015). What twin studies tell us about the heritability of brain development, morphology, and function: A review. *Neuropsychology Review*, *25*(1), 27-46.

Johnson, B. T., Redding, C. A., DiClemente, R. J., Mustanski, B. S., Dodge, B., Sheeran, P., & ... Fishbein, M. (2010). A network-individual-resource model for HIV prevention. *AIDS And Behavior*, *14*(Suppl 2), 204-221.

Kaplan, G. A., Everson, S. A., & Lynch, J. W. (2000). The Contribution of Social and Behavioral Research to an Understanding of the Distribution of Disease: A Multilevel Approach. In B. D. Smedley and S. L. Syme (Eds.), *Promoting health: Intervention strategies from social and behavioral research* (pp. 37-80). Washington, DC: National Academy Press.

Kasabov, N., Jain, V., & Benuskova, L. (2008). Integrating evolving brain-gene ontology and connectionist-based system for modeling and knowledge discovery. *Neural Networks*, *21*, 266-275.

Klein, K. J., & Kozlowski, S. W. J. (2000). A multilevel approach to theory and research in organizations: Contextual, temporal, and emergent processes. In K. J. Klein & S. W. J. Kozlowski (Eds.), *Multilevel theory, research, and methods in organizations: Foundations, extensions, and new directions* (pp. 3-90). San Francisco, CA: Jossey-Bass.

Kohl P, Noble D, Winslow R, Hunter PJ (2000) Computational modelling of biological systems: Tools and visions. *Philosophical Transactions of the Royal Society A, 358*, 579–610.

Lehrman, D. S. (1970). Semantic and conceptual issues in the nature-nurture problem. In L. R. Aronson, E. Tobach, D. S. Lehrman, & J. S. Rosenblatt, (Eds.), *Development and evolution of behavior* (pp. 17-52). San Francisco, CA: Freeman.

Lewis, M. D., & Todd. R. M. (2007). The self-regulating brain: Cortical-subcortical feedback and the development of intelligent action. *Cognitive Development, 22,* 406-430.

Lich, K. H., Ginexi, E. M., Osgood, N. D., & Mabry, P. L. (2013). A call to address complexity in prevention science research. *Prevention Science*, *14*(3), 279-289. doi:10.1007/s11121-012-0285-2

Luke, D.A. (2004) Multilevel Modeling. *Quantitative Applications in the Social Sciences, 143,* 1-7.

Luo, W., & Kwok, O. (2009). The impacts of ignoring a crossed factor in analyzing cross-classified data. *Multivariate Behavioral Research*, *44*, 182-212.

MacLean, P. D. (1990). *The triune brain in evolution: Role in paleocerebral functions*. New York: Plenum.

Magnusson, D., & Stattin, H. (1998). Person-context interaction theories. In W. Damon and R. M. Lerner (Eds.), *Handbook of Child Psychology: Vol. 1*. *Theoretical Models of Human Development* (pp. 685-759). New York: Wiley.

Magnusson, D. (1985). Implications of an interactional paradigm for research on human development, *International Journal of Behavioral Development, 8,* 115-137

Magnusson, D. (2003). The person approach: Concepts, measurement models, and research strategy. In W. Damon (Series Ed.), S. C. Peck, & R. W. Roeser (Vol. Eds.), New *Directions for Child and Adolescent Development: Vol. 101. Person-centered approaches to studying human development in context* (pp. 3-24). San Francisco: Jossey-Bass.

Manuck, S. B., & McCaffery, J. M. (2014). Gene-environment interaction. *Annual Review of Psychology*, *65,* 41-70.

Mathieu, J. E., & Chen, G. (2011). The etiology of the multilevel paradigm in management research. *Journal Of Management*, *37*(2), 610-641.

Mayr, E. (1961). Cause and effect in biology. *Science, 134*, 1501-1506.

McCulloch, W. S. (1945). A heterarchy of values determined by the topology of nervous nets. *Bulletin of Mathematical Biophysics, 7,* 89-93.

McEwen, B. S. (2001). From molecules to mind: Stress, individual differences, and the social environment. In A. R. Damasio, A. Harrington, J. Kagan, B. S. McEwen, H. Moss, R. Shaikh, ... R. Shaikh (Eds.) , *Unity of knowledge: The convergence of natural and human science* (pp. 42-49). New York: New York Academy of Sciences.

Mesulam, M. M. (2000): *Principles of Behavioral and Cognitive Neurology.* Oxford, England: Oxford University Press.

Meyers, J. S., & Beretvas, S. N. (2006). The impact of inappropriate modeling of cross-classified data structures. *Multivariate Behavioral Research, 41*(4), 473-497.

Mezuk et al., 2013;

Molenaar, P. C. M. (2004). A manifesto on psychology as idiographic science: Bringing the person back into scientific psychology, this time forever. *Measurement, 2,* 201-218.

Noble, D. (2012). A theory of biological relativity: No privileged level of causation. *Interface Focus, 2*, 55–64.

Norman, G. J., DeVries, A. C., Cacioppo, J. T., & Berntson, G. G. (2011). Multilevel analysis of stress. In R. J. Contrada, A. Baum, R. J. Contrada, A. Baum (Eds.), *The handbook of stress science: Biology, psychology, and health* (pp. 619-634). New York: Springer.

Parker, D., & Srivastava, V. (2013). Dynamic systems approaches and levels of analysis in the nervous system. *Frontiers in Physiology, 4*(15), 1-15.

Pattee, H. H. (1973). The physical basis and origin of hierarchical control. In H. H. Pattee (Ed.), *Hierarchy theory: The challenge of complex systems* (pp. 71-108). New York: Braziller.

Peck, S. C. (2007). TEMPEST in a gallimaufry: Applying multilevel systems theory to person-in-context research. *Journal of Personality, 75*, 1127-1156.

Pedhazur, E. J., & Schmelkin, L. P. (1991). *Measurement, design, and analysis: An integrated approach (student ed.)*. Hillsdale, NJ: Erlbaum.

Pellmar, T. C., & Eisenberg, L. (Eds.) (2000). Bridging disciplines in the brain, behavioral, and clinical sciences. Committee on Building Bridges in the Brain, Behavioral, and Clinical Sciences; Division of Neuroscience and Behavioral Health. Washington, DC: National Academy Press.

Phillips, P. C. (2008). Epistasis—the essential role of gene interactions in the structure and evolution of genetic systems. *Nature Reviews. Genetics*, *9*(11), 855–867.

Plomin, R., DeFries, J. C., Knopik, V. S., & Neiderhiser, J. M. (2016). Top 10 replicated findings from behavioral genetics. *Perspectives On Psychological Science*, *11*(1), 3-23.

Polderman, T. J. C., Benyamin, B., de Leeuw, C. A., Sullivan, P. F., van Bochoven, A., Visscher, P. M., Posthuma, D. (2015). Meta-analysis of the heritability of human traits based on fifty years of twin studies. *Nature Genetics, 47*(7), 702-709.

Richters, J. E. (1997). The Hubble hypothesis and the developmentalist's dilemma. *Development and Psychopathology, 9,* 193-229.

Roco, M. C., & Bainbridge, W. S. (2002). Overview: Converging technologies for improving human performance: Nanotechnology, Biotechnology, Information Technology, and Cognitive Science (NBIC). NSF/DOC-sponsored report. http://www.wtec.org

Rydin, Y., Bleahu, A., Davies, M., Davila, J. D., Friel, S., de Grandis, G., . . . Wilson, J. (2012). Shaping cities for health: Complexity and the planning of urban environments in the 21st century. *The Lancet, 379* (9831), 2079-2108.

Salthe, S. N. (1985). *Evolving hierarchical systems: Their structure and representation.* New York: Columbia.

Salthe, S. N. (1993). *Development and evolution: Complexity and change in biology.* Cambridge, MA: Massachusetts Institute of Technology.

Sameroff, A. J. (1983). Developmental systems: Contexts and evolution. In W. Kessen (Ed.), P. H. Mussen (Series Ed.), *Handbook of child psychology: Volume 1. History, theory, and methods*. (pp. 237-294). New York: Wiley.

Sameroff, A., Gutman, L. M., & Peck, S. C. (2003). Adaptation among youth facing multiple risks: Prospective research findings. In S. S. Luthar (Ed.), *Resilience and vulnerability: Adaptation in the context of childhood adversities* (pp. 364-391). New York: Cambridge University Press.

Schneirla, T. C. (1949). Levels in the psychological capacities of animals. In R. W. Sellars, V. J. McGill, & M. Farber (Eds.), *The quest of modern materialism* (pp. 243-286). New York: MacMillan.

Schölmerich, V. L. N., & Kawachi, I. (2016). Translating the Socio-Ecological Perspective into Multilevel Interventions: Gaps Between Theory and Practice. *Health Education & Behavior, 43*(1), 17-20.

Schulz, A. J., Israel, B.A., Coombe, C., Gaines, C., Reyes, A., Rowe, Z. …Weir, S. (2011). A community-based participatory planning process and multilevel intervention design: Toward eliminating cardiovascular health inequities. *Health Promotion Practice , 12*(6): 900-912 .

Sherman, P. W. (1988). The levels of analysis. *Animal Behaviour*, *36*(2), 616-619.

Shonkoff, J. P. (2010). Building a new biodevelopmental framework to guide the future of early childhood policy. *Child Development*, *81*(1), 357-367.

Shonkoff, J. P., & Phillips, D. A. (2000). *From neurons to neighborhoods: The science of early childhood development*. Washington, DC: National Academy Press.

Simon, H. A. (1996). *The sciences of the artificial* (3rd Ed.). Cambridge, MA: MIT Press.

Slavich, G. M., & Cole, S. W. (2013). The emerging field of human social genomics. *Clinical Psychological Science*, *1*(3), 331-348.

Stanovich, K. E. (2012). Chapter 9: The misguided search for the "magic bullet": The issue of multiple causation. In K. E. Stanovich (Ed.), *How to think straight about psychology*, 10th Ed. (147-154). Essex, UK: Pearson.

Stark, D. (2001). Heterarchy: Exploiting ambiguity and organizing diversity. *Brazilian Journal of Political Economy, 21*(1), 21-39.

Steg, L., Buunk, A. P., & Rothengatter, T. (2008). *Applied social psychology: Understanding and managing social problems*. New York: Cambridge University Press.

Taylor, P. J. (2010). Three puzzles and eight gaps: What heritability studies and critical commentaries have not paid enough attention to. *Biology & Philosophy, 25*:1-31.

Taylor, P. J. (2015). Distinctions that make a difference? An essay review of Beyond Versus: The struggle to understand the interaction of nature and nurture, by James Tabery. *Studies in History and Philosophy of Biological and Biomedical Sciences, 51*, 70-76.

Thakar, J., Pilione, M., Kirimanjeswara, G., Harvill, E.T., & Albert, R. (2007). Modeling systems-level regulation of host immune responses. *PLoS Computational Biology, 3*(6), e109.

Thienpont, K., & Verleye, G. (2004). Cognitive ability and occupational status in a British cohort. *Journal of Biosocial Science*, *36*(3), 333-349.

Tinbergen, N. (1963). On aims and methods of ethology. *Zeitschrift für Tierpsychologie,* 20, 410-433.

Trickett, E. J., & Beehler, S. (2013). The ecology of multilevel interventions to reduce social inequalities in health. *American Behavioral Scientist*, *57*(8), 1227-1246.

Trochim, W.M., Cabrera, D.A., Milstein, B., Gallagher, R.S., & Leischow, S.J. (2006). Practical challenges of systems thinking and modeling in public health. *American Journal of Public Health, 96*(3), 538-546.

Tucker-Drob, E. M., Briley, D. A., & Harden, K. P. (2013). Genetic and environmental influences on cognition across development and context. *Current Directions In Psychological Science*, *22*(5), 349-355.

Turkheimer, E. (2016). Weak genetic explanation 20 years later: Reply to Plomin et al. (2016). *Perspectives On Psychological Science*, *11*(1), 24-28.

Urban, J. B., Osgood, N. D., & Mabry, P. L. (2011). Developmental systems science: Exploring the application of systems science methods to developmental science questions. *Research In Human Development*, *8*(1), 1-25.

VanderWeele, T. J. (2012). Invited commentary: Assessing mechanistic interaction between coinfecting pathogens for diarrheal disease. American Journal of Epidemiology, 176(6), 396-399.

Voit, E. O., Qi, Z., & Miller, G. W. (2008). Steps of modeling complex biological systems. *Pharmacopsychiatry*, *41*(Suppl1), S78-S84.

von Eye, A., & Bergman, L. R. (2003). Research strategies in developmental psychopathology: Dimensional identity and the person-oriented approach. *Development and Psychopathology, 15*, 553-580.

Weeks, M. R., Li, J., Liao, S., Zhang, Q., Dunn, J., Wang, Y., & Jiang, J. (2013). Multilevel dynamic systems affecting introduction of HIV/STI prevention innovations among Chinese women in sex work establishments. *Health Education & Behavior*, *40*(1, Suppl), 111S-122S.

Wimsatt, W. C. (2013). Articulating Babel: An approach to cultural evolution. *Studies in History and Philosophy of Biological and Biomedical Sciences, 51*, 563-571.

Worboys, M. (2000). *Spreading germs: Disease theories and medical practice in Britain, 1865-1900*. Cambridge, UK: Cambridge University Press.

Appendix A: Summary of Multilevel Systems Theory

In this appendix, I briefly summarize some more formal approaches to multilevel systems and how they can help us solve the theoretical, methodological, and practical challenges associated with addressing complex social problems, particularly those that have been framed as gene-by-environment interaction problems. The primary goal is to illustrate how and why we can move away generic levels-of-analysis approaches and toward approaches that address specifically several different kinds of multilevel systems.

The initial theoretical problem associated with addressing complex social problems, such as the social class attainment gap, is how to frame questions about social problems in a way that represents both the causally-relevant features of the problem and the interrelations among these features. Put simply, if our theoretical framing (e.g., gene-environment interactions) excludes reference to potentially-relevant causal factors (e.g., subjective perceptions), then we are likely to neglect and misunderstand the role those excluded factors play in creating, maintaining, and remediating the social problems we are trying to eliminate. In this regard, the generic levels-of-analysis approach appears to be insufficient because, although it signals *that* there are multiple "levels" involved (e.g., genes, environments), it generally provides little information about what those levels are, where they are situated in relation to other levels, and how units of analysis distributed across those levels are interrelated both within and across levels. In analytic terms, this would be like having no idea whether your model should be set up as a standard, nested, or cross-classified model. In practical terms, this would be like having no idea which was more important to a successful roadtrip, gasoline or hubcaps. In other words, by relying on a generic levels-of-analysis approach, we are left with only a partial view of the system we are studying, and we have no way of knowing whether or not, or in what way, the excluded parts are necessary or helpful for understanding the problem or any potential solutions.

In order to understand more clearly the units and levels of analysis implicated by any given social problem, we might begin by trying to describe more explicitly the kinds of biological, psychological, and social factors believed to be associated with that social problem. For example, if we were asked to help explain and remediate the social class attainment gap, then we would need to define the social class attainment gap and whatever factors were hypothesized to influence that gap (e.g., genes, physiological functioning, psychological attributes, social capital, intergenerational processes). However, to unambiguously describe such factors (and their interrelations), it would help to be able to anchor those descriptions to a common frame of reference. In multilevel systems terms, this means moving away from discipline-centric forms of description and toward transdisciplinary forms of description; that is, descriptions that use the same terms and meanings across disciplines or that, at minimum, include reference to a common framework capable of disambiguating any potentially overlapping terms or meanings.

In order to get a sense of what such a multilevel description (e.g., of the social class attainment gap and its associated factors) might look like, we first need to consider more carefully what we think we know about multilevel systems. For example, if we suspect that the social class attainment gap involves gene-environment interactions, then we may need to define potentially-relevant factors by reference to levels of analysis ranging from the molecular to the ecological, including (but not limited to): molecular (genetic), cellular (neural), organ (brain), organism (person), small group (family, business), group of small groups (social service organizations, institutions), small geographic regions (small geo groups (nbhd, cities, counties).

Although it may be easy to agree that social problems implicate multiple levels of analysis, it is apparently difficult to agree on what constitutes a level of analysis. Many investigators use a *levels* concept, but there are few corresponding attempts to describe these concepts by reference to an overarching multilevel systems theory framework. Part of the problem is that there are few well-developed multilevel systems frameworks to reference; a bigger part of the problem is that there are few discussions about how to conceptualize levels and their corresponding units of analysis. For example, although the levels-of-analysis concept is popular, there have been few attempts to distinguish it from, or interrelate it to, several other equally compelling multilevel systems concepts, such as “levels of organization” (Campbell, 1990), “levels of representation” (Schneirla, 1949), or “levels of integration” (Grene, 1988).

Levels of organization. Despite the multilevel systems meta-problem of there being no consensus about the nature of multilevel systems, the scientific literature has generally converged around the assumption of a unidimensional series of hierarchical levels, or scales of magnitude, ranging from the sub-atomic to the super-galactic. This series of materially-nested part-processes has been more recently referred to as the default *hierarchy of nature* (Salthe, 1985), the *mainstream hierarchy* (Aronson, 1987), and the *hierarchy of life* (Ahl & Allen, 1996). Segments of this hierarchy most proximal to the concerns of social scientists have been variously termed *psychosocial* (Erikson, 1968), *biopsychosocial* (Engel, 1977), *bioecological* (Bronfenbrenner & Ceci, 1994), *neurons to neighborhoods* (Shonkoff & Phillips, 2000), *molecules to mind* (McEwen, 2001), and *cells to society* (Gehlert et al., 2007). Whereas the physical and biological sciences are based on a fairly consensual understanding of a series of materially-nested physical and organic *levels of organization* (LoOrg) (e.g., molecules, cells, organs), there is minimal consensus within the social sciences about (a) the names, nature, and ranges of relevant LoOrg, particularly those extending beyond the organism; (b) the units of analysis characterizing LoOrg; and, most troubling, (c) the extent to which units of analysis map clearly onto to any particular LoOrg scheme (Peck, 2007; Salthe, 1985).

Despite this lack of consensus, we can nevertheless use the basic LoOrg concept to illustrate the extent of complexity implied by most social problems and corresponding prevention and intervention efforts. For example, a typical levels of organization approach to the biology of the human organism involves at least six different levels of organization (e.g., atoms, molecules, organelles, cells, organs, organisms), each with its own set of level-specific units of analysis that differ qualitatively across levels (Salthe, 1985). In this view, we are confronted immediately with several conceptual and analytic challenges, one of which involves the difference between the dynamic relations among units of analysis within a given LoOrg and the dynamic relations between units of analysis at different LoOrg. For example, the factors governing the ways cells interact with each other within organs differ from the factors governing the ways cells interact with the underlying organelles and macromolecules from which they are composed.

Close analysis of a wide variety of such intra- and inter-LoOrg relations indicates that similarly distinct factors are found across the full range of LoOrg. Despite these many different factors, however, several key principles that apply across the full range of LoOrg have been identified. One of these principles is that the dynamic relations among units of analysis *within* a given LoOrg are characterized by a level-specific timescale (Pattee, 1973). For example, the timescale useful for understaning the rates at which adjacent cells interact (e.g., milliseconds) differ radically from the timescale useful for understaning the rates at which adjacent people interact (e.g., seconds).

These timescales (or rates) vary systematically across LoOrg by orders of magnitude, such that a *cogent moment* (Salthe, 1993) at focal level L (i.e., the typical rate of interactions at level L) corresponds to many cogent moments at lower-level L-1 but only a fraction of a cogent moment at higher-level L+1. These distinct timescales, coupled with the equally distinct size typical of the level-specific units of analysis, reveals "a real break, or boundary, in the world at every jump *across* a level [of organization]" (Salthe, 1985, p. 122), and these between-level differences highlight the extent to which *intra*-level relations among units of analysis are generally stronger than *inter*-level relations among units of analysis (Simon, 1996).

One of the primary implications of this view of inter-level relations is that units of analysis at a given level of organization (e.g., organelle) tend to interact weakly with those at adjacent levels (e.g., molecules or cells) and not at all with those on non-adjacent levels (e.g., atoms or organisms). This view of the interrelations among units of analysis within a hierarchically-nested LoOrg framework highlights a core set of *constraints* on how we might understand interactions among units across LoOrg and has been referred to as the principle of "nontransitivity of effects across levels" (Salthe, 1993, p. 45). In short, this principle indicates that causal effects generally flow across LoOrg only via adjacent levels; that is, they do not skip over levels. For example, the effects of molecules on organs are generally mediated fully by cells. In this view, we can see clearly at least part of the complex chain of events indicating that genes can have no direct effect on behavior; that is, whatever effects genes have on behavior are likely mediated by inter-level relations involving macromolecules, organelles, cells, tissues, and organs. Further, given that these principles appear to reflect laws of nature, they almost certainly manifest similarly at higher (i.e., social) LoOrg; meaning, they have relevance for understanding social problems or their remediation, even if, at this point, there have been few if any attempts to determine what that relevance might be (a situation that is perhaps akin to medical practice prior to germ theory; e.g., Worboys, 2000).

Although the precise specification of LoOrg and their corresponding units of analysis vary somewhat across sub-disciplines of biology, taken as a whole they tend to be quite consistent and conform to the same set of basic principles (e.g. materially-nested hierarchical organization, spatial and temporal features that vary by orders of magnitude, and nontransitivity of effects across levels). In these terms, and assuming we could describe social LoOrg with the same specificity that we can describe biological LoOrg, tracing an effect from policy to epigenetics to a social class attainment gap would require attending explicitly to more than six, and probably upwards of a dozen, different LoOrg. Further, given our relative ignorance about the mechanisms that transfer effects between these LoOrg, coupled with the constraints we do know about (e.g., that effects generally travel only between adjacent levels), we should not be surprised by how little we know about the extent to which the effects of any given policy decision (e.g., free public education) will cascade through these LoOrg to produce the desired effects (e.g., favorable gene expression or the elimination of social class attainment gaps).

Levels of representation. Unfortunately, as if this situation was not already complicated enough, there are also reasons to believe that any such unidimensional LoOrg framework alone will be an insufficient basis for guiding theory, methods, and practices; that is, we also know that many multilevel systems are characterized better as heterarchically- than hierarchically-organized systems (Berntson &

Cacioppo, 2008; Bruni & Giorgi, 2015; Crumley, 1995, 2015; Lewis & Todd, 1997; MacLean, 1990; McCulloch, 1945; Mesulam, 2000; Salthe, 1985, 1993; Stark, 2001). For example, the evolution, development, and functioning of the human brain highlight both the limits of LoOrg schemes (e.g., not all multilevel systems are hierarchically nested) and why additional multilevel systems are necessary for understanding the relations among so-called biological, psychological, and social phenomena.

Heterarchical brain organization indicates that the relations among constructs centered in different areas of the brain tend to be *functionally interconnected* (e.g., as networks) even though they are not materially nested. For example, the biological evolution of the brain can be described by the emergence of a relatively clear set of *levels of representation* (LoRep) marked by increasingly flexible processing capacities as we move up the neuroaxis from the brain stem to the prefrontal cortex (Berntson & Cacioppo, 2003; Bronson, 1965; Derryberry & Tucker, 1991; Herrick, 1949; Lewis & Todd, 1997; MacLean, 1990; Norman et al., 2011; Schneirla, 1949), and behavior tends to be influenced by simultaneous inputs (i.e., parallel processing) from these networked areas of the brain. In conventional dual-systems terms (e.g., automatic-controlled, experiential-rational, reflexive-reflective), this means that any given behavior (e.g., singing a pride song, or using salty slang) can be influenced simultaneously by long-held associative memories about the pleasure and meaning of singing the song (or using salty slang) together with newly-formed beliefs about where and when singing the song (or using salty slang) is deemed most socially acceptable. In other words, behavior is multiply-determined and, in contrast to the non-transitive relations among LoOrg, the relations among LoRep are characterized by transitive relations; that is, the effects of a given LoRep (L1) can bypass another LoRep (L2) to have a direct effect on a third LoRep (L3).

Similar to the under-developed specification of extra-organismic LoOrg, we know much less about extra-organismic LoRep than we do about intra-organismic LoRep, and these knowledge gaps likely have severe consequences for our ability to design and implement the most efficient prevention and intervention programs. The main reason for expecting such knowledge gaps to undermine intervention design and implementation is that social environments appear to be at least as complicated as biological or psychological environments. For example, from a LoOrg perspective we can view social environments as a series of materially-nested collections of individuals and groups (e.g., families within neighborhoods within communities, or employees within departments within organizations). However, from a LoRep perspective, we must also contend with heterarchical dynamics generated by the norms, rules, and laws specific to social groups defined less by material nesting and more by psychological identification (e.g., beliefs about religion, politics, racial/ethnic, sex/gender, etc.).

One of the implications of such heterarchical views of multilevel systems for understanding complex social problems is that LoOrg, no matter how complex they may seem to the casual observer, are almost certainly an overly-simplistic representation of a far more complex system. In other words, whatever understanding of the relations among biological, psychological, and social systems we gain from LoOrg perspectives will almost certainly need to be modified by reference to the pervasive role LoRep (and other) heterarchical systems likely play in governing the relations among these systems, hence in creating, sustaining, and ameliorating social problems like social class attainment gaps. The mere presence of LoRep suggests that both LoOrg and LoRep have implications for understanding social problems and their solutions; however, understanding these implications depends on understanding not only LoOrg and LoRep but the interrelations between LoOrg and LoRep. However, developing a systematic understanding of these complex systems is a work (barely) in progress. Hence, understanding their implications for social problems and solutions appears to be more of a future promise than a current reality. Nevertheless, we know enough about LoOrg, LoRep, and their interrelations to help us appreciate (a) how they can be used to add specificity to the generic levels-of-analysis concept, (b) how this specificity can help us understand the extent to which diverse disciplinary approaches to defining and addressing social problems may be similar or different (despite whatever appearances are suggested by the similar or different terms used to describe these approaches) and, consequently, (c) how any given component (e.g., genes) could likely impact these social problems and solutions (i.e., as one component of a multiply-determined system). In short, given what we know about multiply-determined systems (a lot) and genetic influences on complex "traits" (not much), it is unlikely, although not impossible, that any one component so determines social problems like the social class attainment gap that prevention and intervention would be futile.