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Social Ecology, Genomics, and African American Health: A Nonlinear Dynamical Perspective

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Abstract

This article offers a model that clarifies the degree of interdependence between social ecology and genomic processes. Drawing on principles from nonlinear dynamics, the model delineates major lines of bifurcation involving people's habitat, their family health history, and collective catastrophes experienced by their community. It shows how mechanisms of resource acquisition, depletion, and preservation can lead to disruptions in basic metabolism and in the activity of cytokines, neurotransmitters, and protein kinases, thus giving impetus to epigenetic changes. The hypotheses generated from the model are discussed throughout the article for their relevance to health problems among African Americans. Where appropriate, they are examined in light of data from the National Vital Statistics System. Multiple health outcomes are considered. For any one of them, the model makes clear the unique and converging contributions of multiple antecedent factors.

Keywords

health; social-ecological factors; genome; African Americans

There is a basic axiom in mathematics that any problem, if improperly defined, will remain intractable, with no clear and efficient solution in sight. The unsatisfactory condition of health care for African Americans represents in a sense such a problem. Its current definition is often based on simple comparisons of disease prevalence in White and African American populations, as if the health profile of Whites could or should serve as a normative reference. This approach ignores the real possibility that, in some cases, parity with Whites may not be a desirable health outcome for African Americans. For instance, the rate of suicide is much higher among European Americans than among African Americans; therefore, equality of outcome is clearly not advantageous in this area. Second, the approach implies that, when the prevalence of a disease is similar in the African American and White community, there is perhaps no more cause for concern. But a degree of common misery cannot be a substitute for an adequate standard of health. Third, the approach does not allow for a comprehensive or in-depth understanding of the causal pattern determining disease, life expectancy, and death in the African American community. An almost exclusive focus on Black-White comparisons can only address the distal factors contributing to health conditions. It does not explain the proximal mechanisms by which disease occurs or health can be restored and maintained. Consequently, the approach does not open the door for the exploration of more effective preventive and treatment measures, or for engineering new ways of delivering care to a community facing a number of daunting health problems.

These challenges call for the design of new models (Anderson, 1999) for studying the health status of African Americans. One paradigm that has received quite a bit of attention lately is that of social ecology. Generally speaking, ecology refers to the environmental conditions under which an organism emerges and sustains itself. Because human activity can markedly alter these environmental conditions, social ecology looks beyond natural resources toward the set of opportunities, constraints, and risks generated through sociocultural organization. Sallis and Glanz (2006) have characterized such a transformed milieu as the *built environment*. The social-ecological framework has been applied to health most extensively by Stokols (1992), who argued that “the healthfulness of a situation and the wellbeing of its participants are influenced by multiple facets of both the physical environment (e.g., geography, architecture, and technology) and the social environment (e.g., culture, economics, and politics)” (p. 7).

Studies conducted lately about gene-environment interaction are congruent, to a certain extent, with the social-ecological paradigm. Arguments about health differences that even mention genetics must be put forth with great care, not because of their supposedly explosive social connotations, but to avoid the quicksands of a monofactorial, monogenic approach to disease. Extant research is quite clear that few diseases or behaviors are rooted in the activity of a single gene. Mindful of this very point, the present article proposes a model that seeks to bring together ecological and genomic factors. This effort is worthwhile at a time when gene therapy is pushing the frontiers of medicine: For instance, recent research advances on *induced pluripotent stem cells* (adult cells that can perform in ways similar to embryonic cells) hold the potential for bringing relief to people who suffer from sickle-cell anemia—a disease that afflicts more than 1 in 700 African Americans (Burke, 2004). Work on a series of genes including ERG, DD3, and especially PCGEM1 (Petrovics, Zhang, Makarem, & Street, 2004) seems to be promising for the diagnosis of and survival from prostate cancer, which stands as the deadliest form of malignancy among African American men with a rate of 120 per 100,000 (Blot, 2004).

Traditionally, genetic and ecological explanations of behavior or of the root causes of health and illness have been presented as competing rather than complementary frames of reference. Can the tension between the two perspectives ever be resolved? A number of scholars, particularly members of minority groups, have tended to view research findings from genetics with suspicion (Washington, 2007), because observations about genetic diversity have been too often distorted into pronouncements about genetic superiority. But rapid progress in genomic discoveries has practically demolished every premise of any argument about genetic superiority of one group over the other: (a) The sequencing of the human genome has clearly established that, for 99.9% of the genome, all human beings are similar (Guttmacher & Collins, 2004). (b) The bulk of available scientific evidence tends to corroborate the hypothesis that the human species, as we know it today, emerged from Africa and spread out to gradually occupy the other parts of the world (Johanson & Shreeve, 1989). (c) There is greater genetic diversity among the populations of Africa than among people of the other continents. According to Cavalli-Sforza and Feldman (2003), the genetic diversity observed outside of the African continent is actually a subpattern of the diversity inside that continent. (d) A greater proportion of the nucleotide polymorphisms observed among people of European origin is likely to lead to disease than it is the case among people of African descent (Lohmueller, Indap, Boyko, & Bustamante, 2008). (e) The chain of amino acids that constitutes the DNA is not immutable but continues to periodically undergo change or damage. It is only when the organism cannot autonomously repair this damage that a genetic mutation occurs. (f) Last but not least, genes are sensitive to environmental variations, particularly in the womb and during the early stages of cell development (Encha-Razavi, Folkerth, & Harding, 2004).

Empirical Challenges from Health Profiles

Many analyses of health disparities are based on differential prevalence of various diseases across populations. Interesting as such comparisons may be, they are rendered somewhat less informative because of redundancies in the data. For instance, diabetes is a correlate or even a precursor of renal failure. So because of comorbidity, the relative position of a group on the first disease dictates its position on the second disease. Cognizant of this statistical constraint, we began paying attention to data on the leading causes of *death*, as a way of charting a more orderly picture of the most critical health needs. These kinds of vital statistics have been published by the National Center on Health Statistics. Extracting from these data, we provide in Table 1 contrasting profiles for two major demographic groups in the United States (White and African Americans). These profiles highlight both between-group and within-group differences. They make clear the need to think differently about health disparities. Indeed, examining the rate of mortality due to diabetes mellitus for instance, one notices that it is higher in the African American population (34.8 per 100,000) than among Whites (24.6 per 100,000). But chronic lower respiratory problems affect the White population (49.9 per 100,000) much more than they do the African American community (21.5 per 100,000). Death due to septicemia is much higher among African Americans (16.8 per 100,000) than among Whites (11 per 100,000). But the impact of Alzheimer's disease is much more salient among Whites (20.5 per 100,000) than among African Americans (7.7 per 100,000). The within-group comparisons are equally revealing. Malignant neoplasm (cancer) affects many more people than does cerebrovascular disease. While AIDS is devastating to the African American community (with a mortality rate of 22.2 per 100,000), perinatal conditions have an impact no less startling (with a rate of 14.2 per 100,000).

The first lesson from these data is that the health profile of Whites could or should not automatically serve as a normative reference. Secondly, to properly address the health challenges, we need to understand not only the conditions that are conducive to social disparities but also the mechanisms through which exogenous, social factors give rise to endogenous, biological inputs, directly affecting health.

Conceptual Framework

A new model, to be useful, must account for most of the outcomes revealed in the vital profiles presented in Table 1. Keeping these outcomes firmly in sight, we began to step back to gain perspective and try to detect any causal pattern. We thus reviewed a number of studies and examined several existing models of health and disease, built around different sets of causal inputs. One strand of studies looks for causes among psychosocial factors (Adler, Marmot, McEwen, & Stewart, 1999). Another type of studies underscores the role of genes (Guttmacher & Collins, 2004). A third type of studies puts the emphasis on processes in the intrauterine environment (Alcolado, 2006; Casas, Cavalleri, & Bautista, 2006). A fourth strand of studies focuses almost exclusively on causal inputs from the physical environment (Kaplan, 1996). These types of studies seemed particularly useful for the analysis of between-group and within-group differences.

Understanding Between-Group Health Differences

One of the best-known models for evaluating between-group differences is perhaps the one developed by the MacArthur Network on Socioeconomic Status (SES) and Health. As described by Adler and Ostrove (1999), this broad model made clear several important points: (a) Differences in SES lead people to live in very different environments, and shape their emotional as well as cognitive experiences. (b) The type of environment influences the likelihood of exposure to carcinogens and pathogens; it also constrains health behaviors. (c) Emotional and cognitive experiences trigger and modulate neurologic, immune, and

cardiovascular responses. (d) Taken together, these factors contribute to shape an SES gradient for illness and health.

Because some differences in health outcomes tend to persist even after differences in SES have been accounted for, some researchers have turned to the examination of other factors of social ecology, such as racism. Access to health care is restricted not so much as a function of SES but due to racial discrimination. One of the most thought-provoking models in this vein is perhaps the one proposed by Williams (1996). He laid out the case in the following manner: (a) Macro-social factors based on historical conditions, the prevailing political order, and existing legal codes contribute to create a racial ideology that fuels prejudice and discrimination. (b) This racial ideology permeates social status, social roles, and demographic categorizations. (c) Therefore, racism along with the social status indicators operates to exacerbate risk factors such as stress, and to place constraints on resources such as medical care. (d) Psychological effects ensue that compromise both physical and mental health.

Despite their heuristic value, models built only around the access-stress axis turn out to have some serious limitations. First of all, good health indicators do not always track SES in the expected direction. For instance, Murray et al. (2006) have shown that, despite greater levels of poverty, life expectancy is higher for African Americans living in the Mississippi Valley and the Deep South than for their kindred living in more urbanized counties of northern inner cities. When one attempts to understand a broad range of health conditions, the models seem adequate to account for differences in one common type of disease (cardiovascular complications, specifically), but appear less useful for approaching other types of ailments afflicting African Americans (glaucoma or sickle-cell anemia, for instance). Sometimes, the main prediction from this type of models cannot find any support through empirical analyses: For instance, the relationship between perceived racism and blood pressure is frequently not statistically significant (Jones, Harrell, Morris-Prather, Thomas, & Omavale, 1996).

We drew two conclusions from these perplexing findings: (a) The principle of social hierarchy, (on which many popular social models base their validity), while perhaps necessary, is certainly not sufficient to explain differences in health status. (b) The relations between psychosocial factors and health outcomes may not be linear.

Understanding Within-Cell Conditions

An exploration of social factors does not preclude an examination of within-cell conditions. One paradigm relevant to this examination is that of gene-environment interaction. Genomics is the study of the functions of genes and their interaction with the environment (Guttmacher, Collins, & Drazen, 2004). The personal genome, in any human being, is made up of approximately 25,000 to 35,000 genes. "A gene is a segment of DNA that encodes specific instructions which allow a cell to produce a specific product. This product is typically a protein, such as an enzyme" (Draghici, 2003, p. 8). It is known, based on current data that about 2% of the human genome encodes for proteins which carry out most life functions. A protein represents a string of different amino-acid molecules, which fold over in a specific way to perform a very definite function. If a cell generates a large amount of a certain protein, the associated gene is deemed to have a high level of expression. Draghici (2003) points out that "each type of cell (i.e., tissue) will be characterized by a different pattern of gene expression levels, i.e., each type of cell will produce a different set of proteins in very specific quantities" (p. 13). Under normal circumstances, gene expression is the result of a straight conversion process in which information is copied from DNA to RNA into proteins. The conversion involves two steps: transcription (from DNA to RNA) and translation (from RNA to proteins).

Chemical damage may take place when the DNA sequence is being copied. The genome is not made of a set of static parts but of dynamic elements that are in interaction with one another and constantly undergoing change. The genome has the internal capacity to repair such damage. But if, for one reason or another, the repair is not successful, this gives rise to a somatic mutation, leading to a change in function for the gene. An alteration in one nucleotide in the genome is known as a single nucleotide polymorphism (SNP). According to Korf (2004), in the early part of this decade, no less than 2 million gene variants or SNPs had been identified. They contribute to the formation of alternate metabolic pathways.

There are several lessons that we have learned from reviewing gene-environment interaction studies. First of all, genes by themselves cannot tell the whole story: Even the DNA profiles of twins, which are virtually identical at birth, come to differ over time, thus varying the odds that they would develop the same diseases (Fraga, Ballestar, Paz, & Esteller, 2005). Secondly, the same genetic change along a chromosome can ultimately have quite different health manifestations. Third, the process of converting DNA into protein opens the door to the influence of exogenous factors. Fourth, the interaction of a gene with other genes appears to be “chaotic”: For instance, in schizophrenia, the genetic glitches implicated are diverse, suggesting multiple unique pathways rather than a single common one to the disease (Walsh, McClellan, & McCarthy, 2008).

The Nonlinear Perspective

We built an integrated framework from apparently disparate elements of the various existing models mentioned earlier. Apparent contradictions in reported findings led us to the idea that any breakdown in health arguably represents a nonlinear phenomenon. At a minimum, it is a qualitative shift from a satisfactory to a detrimental condition. In general, for a nonlinear dynamical event to occur, two or more systems must be active and placing constraints on one another (Young, 1995). In the case of health and disease, the causal inputs seem to fall into three broad subsystems: a biological subsystem, a psychosocial subsystem, and a spatio-temporal subsystem. We drew on principles of nonlinear dynamics (Goerner, 1995) to bring the subsystems into one totality (described in nonlinear parlance as a *single phase space*) and to explain their functional interdependence.

Some aspects of health have been previously explored for their nonlinear dynamics, at least in part. For instance, Mazanov and Byrne (2006) have analyzed substance abuse in reference to catastrophe theory. The current conceptualization pushes forward with these types of exploration. First of all, to deal with the complexity of the subsystems alluded to above, we hypothesize that, within each of them, there exist certain elements that act as mediators while others behave as *attractors*. In very simple terms, an attractor helps set the range or limits within which an activity may vary. We tentatively hypothesize that gene regulation may act as such an attractor within the biological subsystem. Within the psychosocial subsystem, a person's social network or, more specifically, sustained harmonious contact may very well serve in that capacity.

The resulting model, dubbed *INGAM* (for identity networks, genome, and affect as modulators of health), is presented in Figure 1. The pathways along which different causal inputs exert their influence on health are delineated within each subsystem. The major points of interconnection and mechanisms of interdependence are then discussed.

The INGAM Model

The INGAM model posits that ancestry is at the foundation of any comprehensive model of health and illness. This is the first common point of linkage between all causal inputs; in nonlinear dynamical terms, this is called the *seed* of the system. Ancestry refers to the pattern

of genetic variation that, according to many population geneticists, seems to more or less overlap with continental boundaries. In and of itself, continental ancestry is *not* responsible for extensive genotypic differences between people from different regions of the world. As mentioned earlier, for 99.9% of the genome, human beings are exactly alike. But a focus on ancestry allows us to show from the start how even small variations in the initial conditions of a system may give impetus to multiple flows of activities.

The narrow range of variation in the human genome, representing just 0.1% of the total, still amounts to 3 million base pairs in the DNA sequences, as pointed out by Guttmacher and Collins (2004). Differences associated with bases within this range tend to be reinforced and perpetuated as a result of *assortative mating*. The notion of assortative mating refers to the simple fact that isolation because of continental distance makes it more likely that an individual would mate with another person residing in relatively close regional proximity and sharing the same habitat as well as similar phenotypic features (Tishkoff & Kidd, 2004). Assortative mating works to crystallize the association of certain perceptible characteristics with populations from certain regions of the world. Several characteristics come to mind, including skin color, hair texture, or language. In less salient fashion, assortative mating may explain some patterns of allele frequency in certain geographic areas; these patterns increase the probability of replication for mutations that have a potential role in disease.

Ancestry does not simply reveal some commonality in biological heritage. It also points to some shared experience of particular chains of events over the centuries, that is, a distinct historical trajectory. For every population, the chain of events has included from time to time some collective catastrophes. Collective catastrophe can be defined as a natural or man-imposed event of historic proportions that brings death, disease, and destruction, and drastically alters the living conditions as well as the worldview of a community. Such natural disasters include major hurricanes, tsunamis, earthquakes, or volcanic eruptions. The passage of Hurricane Katrina, which devastated New Orleans and the southern gulf coast of the United States in 2005, is a recent example. Man-imposed disasters include sustained acts of war, genocide, enslavement, or nuclear accidents. The Palestinian-Israeli conflict stands out as a modern-day example. The transatlantic slave trade, which depopulated the west coast of Africa, picking up gale force in the early 1500 and lasting for centuries, is another illustration on a larger scale.

The influence of ancestry and its corollaries shapes the internal dynamics of the biological subsystem, the psychosocial subsystem, and the spatiotemporal subsystem.

The Spatiotemporal Subsystem

The spatiotemporal subsystem deals with ecological conditions, the movements of populations within the environment, and the ways in which people group themselves to survive or even prosper in that environment. The major causal inputs here that critically affect health are characteristics of the *habitat*. In the INGAM model, the term habitat speaks first to the climate, altitude, and fertility of broad geographic areas (e.g., tropical vs. temperate climates). It secondarily refers to conditions of living in the home or neighborhood. The latter conditions have been largely the focus in the literature on environment and health. In our view, this approach is too narrow. We propose that the habitat is a dynamically chaotic domain where one can observe disturbances in input that result in disproportional changes in life and health outcomes for entire populations.

There are three primary pathways linking characteristics of the habitat to health outcomes. The first and most direct pathway involves homeostasis, that is, the capacity of the organism to maintain equilibrium by optimally adjusting internal parameters of temperature, as well as the balance of fluids and electrolytes in response to variations in the physical environment. For

instance, when the weather gets hot, a person perspires. Usually only small adjustments are needed. But when external conditions approach the extremes, the delicate feedback mechanism that ensures homeostasis becomes disturbed, and illness may follow. For instance, at high altitude, a person may experience dizziness and nose bleeding. If the temperature exceeds 115° F, a person may get a heat stroke. For people ill-equipped to live in cold climates, the risk comes from temperature variations that may reach subfreezing levels. A change in microgravity (as is the case for astronauts during space flights) may result in dysregulation of the immune system and an increased vulnerability to infections (Wang, Shi, & Denhardt, 2007).

Melanocortins seem to play a role in the relationship between environment and homeostasis. According to Cone (2003), there are five types of melanocortin receptors, which are involved, respectively in pigmentation and protection against ultraviolet rays (MCR1), cortisol production and stress response (MCR2), energy use and internal temperature control (MCR3), appetitive conduct and weight regulation (MCR4), and sebum production for protection against microorganisms in the skin (MCR5).

A second pathway links habitat to health and involves nutrition. The type of land and weather patterns influence the kind of food as well as the abundance and purity of water available to people residing in an area. In times of scarcity, the habitat affects food insecurity or hunger, which may be the greatest daily challenge for a very large number of people around the world. Even in a wealthy nation such as the United States of America, hunger reportedly affects 35 million people.

Diet has been associated with the metabolic syndrome. One clear manifestation of metabolic problems is obesity. The work of McEwen and Seeman (1999) on allostatic load has shed light on a number of other indicators related to cardiovascular health: blood pressure, heart rate, cholesterolemia, and so on. Excessive food portion is certainly a problem. On the other hand, chronic malnutrition may trigger glucose intolerance or a drop in plasma insulin (Martin, 2004).

The third pathway linking the habitat to health outcomes involves exposure to pathogens. As suggested by the McArthur Network model, the settings in which a person resides determine the level and frequency of exposure to particular allergens and pollutants. For instance, air pollution is a known risk factor in urban, industrialized communities (Peters, von Klot, Heier, & Trentinaglia, 2004). Housing conditions for poor people may also expose them to toxic substances. Exposure to paint with a high level of lead or to asbestos in housing for the poor was a worrisome problem in the United States until recently. In developing nations, mosquito bites are a channel for transmission of malaria. Where hygiene standards are not adequate, there is the additional risk from parasites. The pathway from habitat to pathogen exposure to health is nonlinear. Indeed, while some pathogens in the habitat may be detrimental to health at high doses, exposure in small dose may contribute to sensitization and thus boost the immune system. A very small difference in the dosage may be responsible for a qualitative shift.

Exposure to pathogens or parasites presents a series of challenges to the immune system. It triggers a counterreaction that calls into play cytokines (Maier & Watkins, 1998). In addition to their role in boosting T-cell functions and regulating the duration of an inflammatory response, cytokines are implicated in cell-to-cell communication.

The spatiotemporal subsystem connects to the other two subsystems in ways that generate secondary pathways that point to health outcomes. On one hand, a population parameter that we call transiency serves as a bridge between the habitat and the psychosocial subsystem. On the other hand, factors of biosocial identity are at the nexus between habitat and the biological subsystem.

The transiency connector—Within any habitat, there is constant movement of populations. Particularly at times of collective catastrophe, when homes may be destroyed and water sources contaminated, there may be a massive displacement of people. This may be by choice (as people find it more prudent) or by force (if the catastrophe is engineered by war). In a historical perspective, one can think of the transatlantic slave trade (the “Middle Passage”) as an example of forced relocation. The situation of transiency has become a major challenge of our times, one that can be observed in developing as well as industrialized nations. Common examples can be seen in situations of homelessness or of frequent residential mobility. Drastic changes in the labor market may create worker migration and virtually depopulate entire regions. Globally, the phenomenon of boat people or of refuge camps speaks to this social reality. During the exodus and later at the point of resettlement, very large numbers of people move together. Population density is high under such circumstances. Thus are created ghettos and shantytowns where unsanitary conditions threaten health.

In a situation of transiency, it becomes very difficult for people to properly meet their most basic personal needs. As time goes by, they become frazzled, hypervigilant, and unable to engage in any restorative behavior to rebuild their physical and emotional strength. We use the term restorative behavior to subsume sleep, exercise, or meditation. Restorative behavior such as sleep is needed to stay alive. Sleep deprivation for a few days can induce spatial disorientation. In terms of the metabolic response, trouble with sleep has serious consequences on glucose tolerance and evening cortisol levels. As for emotional health, Riddle and Cho (1989) reported that “EEG-verified sleep disturbances were the most sensitive and specific biological abnormalities seen in adults with major depressive disorders, occurring in approximately 90% of the cases” (p. 227). All the effects of sleep deprivation may be due to the imbalance it creates of the hormone melatonin. In addition to its role in controlling the circadian rhythms, melatonin has shown the capacity to enhance the immune system, to bring under control cardiac arrhythmias, and to contribute to the repair of DNA damage (Barrenetxe, Delagrangue, & Martinez, 2004).

The biosocial identity connector—In order to control part of their habitat and ensure survival, people organize themselves in more or less homogeneous groups. Often people identify themselves in reference to a particular place where they were born or raised: I am a small-town boy; I am a West Indian, and so on. Identity emerges from a process whereby an individual self-classifies or is classified by others as member of a particular demographic group in a society. Biosocial identity refers to organismic, physical, and cultural characteristics such as *cline* or “race,” ethnicity, gender, religion, and so on. In the African American community, one must add skin complexion to this list. The general consensus in the allied health fields is that “human races do not exist as biologic entities” (Herman, 1996, p. 8). But given the weight of history, race remains a socially significant (though imprecise or even at times misleading) indicator of group membership.

There is a direct pathway from biosocial identity to nutrition, reflecting the fact that the type of diet and preference for particular staples vary from one ethnic group to the other. A complementary pathway links biosocial identity to health through nutrient imbalance or food intolerance. A good example is lactase intolerance. According to Berkow and Fletcher (1987), “most non-whites in North America gradually lose the ability to digest lactase between the ages of 10 and 20. This affects 90% of Orientals, and 75% of American Blacks and Indians” (p. 796). In contrast, fewer than 20% of people of Northwest European descent are affected by the problem. Nutrient imbalance may be exacerbated as a result of diet. For instance, it appears that the greater a person's consumption of carbonated beverages, the greater intake of sodium or phosphates, and the greater the excretion of calcium.

The role of specific nutrients in health is well known. In the INGAM model, we account for the significance of nutrient imbalance with a pathway to oxidative damage. Such damage to nucleic acids and proteins, as explained by Marnett (2000), implicates radical oxygen species (ROS) and sets the conditions for cancer. For instance, calcium has been tied to protection against the recurrence of polyps in the colon (Heimbürger, 2004).

Dynamics of Psychosocial Factors Influencing Health

Psychosocial factors, as defined here, refer to exogenous resources on which an individual may draw in order to build some *reserve capacity* (Matthews, 2008) necessary to maintain physical as well as mental health. These resources represent a major subsystem of inputs.

The INGAM model argues that the critical mediator between ancestry, collective catastrophe, and psychosocial factors affecting health is cultural leverage. Empirical analyses of the relationship between SES and health have often found the effect size for SES to be significant but more modest than one would expect. Suspecting confounding, some researchers have suggested that perhaps each component of the SES factor be examined separately. Adler and Ostrove (1999) have called for a direct measure of subjective social standing. This is the role we assign to cultural leverage here. Cultural leverage is the degree of access and influence that a person is afforded when dealing with various institutions such as the school system, the banks, the courts, the police, and so on. The concept of cultural leverage sheds light on our understanding of racism. Racism can be seen as an attempt, sometimes violent, to limit a person's or a group's cultural leverage on the basis of perceived racial membership. Clearly, the two concepts are related, but one is much larger in scope than the other. Cleavages in cultural leverage can take different contours away from racial classifications but along tribal, religious, or gender lines.

The INGAM model delineates three pathways, all rooted in cultural leverage, to explain the influence of psychosocial factors on health: One pathway accounts for the acquisition of resources; another accounts for depletion of resources; and the last accounts for preservation of resources.

Acquisition of resources—The role of socioeconomic status. The first channel of psychosocial inputs deals with resource acquisition. The extent of acquisition of resources is most commonly reflected in a person's SES. Socioeconomic status is usually based on education, occupation, and income. Upstream, SES relates perhaps in a feedback loop to cultural leverage: The higher the cultural leverage of a person or a group, the higher their SES. Downstream, SES determines access to medical care. This includes availability of adequate medical facilities, quality or affordability of treatment, continuity of health insurance, and dissemination of health information. Data from the National Health Interview Survey of 2006 indicate that 14.5% of the U.S. population is still without any health insurance at all. Bach, Pham, Schrag, Tate, and Hargraves (2004) have reported that 48.5% of physicians treating African American and 37% of physicians treating European Americans find it difficult to obtain nonemergency hospital admissions for their patients. The factor of medical access should not be evaluated simply for its direct effect. Its more significant role is probably as a potent enabler of another variable, namely, the approach to decision making regarding health care. Where access is restricted, prevention is forfeited or treatment is delayed. Thus, diseases that are silent stalkers (such as hypertension, diabetes, or glaucoma) are given ample time to cause irreparable damage.

Depletion of resources—The role of stress. A person regularly expends a certain amount of resources just to meet the demands of modern life. Cultural leverage influences the depletion of resources. The lower the cultural leverage, the greater the rate of depletion, given the number

of risks that a person in that situation faces daily. The depletion of resources is more commonly manifested as stress. Stress occurs when the demands of a task or situation are deemed disproportional to the resources currently available to a person. Commonly included among the stressors are variables such as privation, family disruptions due to divorce, illness or death of a relative, but also prejudice, neighborhood and workplace harassment, as well as exposure to violence. Drawing from the work of De Kloet (2004), we adopt the view that stress is often accompanied by marked changes in neurotransmission. The reservoir of neurotransmitters includes serotonin, dopamine, acetylcholine, epinephrine and norepinephrine, glutamate, and GABA. Which one of the neurotransmitters will register the greatest change depends on the particular factor that is most potent in a given situation. Stress directly—or more probably the underlying neurotransmitter turnover—affects activity in the hypothalamus. The carryover effects on health can be observed in at least two areas: (a) First of all, chronic stress affects a person's emotional balance. Repeated stressful experiences may lead to personality disorders, that is, patterns of reactions that mark a person's behavior as inflexible and maladaptive. Stress may provoke mood swings, an externalization of inner conflicts, temporary but notable changes in a person's sense of identity, and unfounded somatic complaints (Berkow & Fletcher, 1987). (b) Physiological sequelae from stress, exposure to violence, and inadequate neurotransmission may be manifested at the chromosomal level with a shortening of the telomeres (Song & Leonard, 2000). It has been suggested that telomere shortening may be a signal for cellular senescence whereby groups of cells are struck with gradual incapacity to replicate themselves (Martin, 2004). The aging process may thus begin prematurely. Jones (2001) has suggested that the comparatively shorter life expectancy of African Americans may be a function of premature aging.

Preservation of resources—The role of sustained harmonious contact. Resources that have been depleted because of stress or illness must be replenished, if health is to be safeguarded. A person's social network, that is, a circle of reliable, trusted relatives, and friends, plays a critical role in that regard. Social support is indexed in the INGAM model as sustained harmonious contact, for it is not so much the size of the social network that is important, but its stability and integrity. The weight of cultural leverage should not be underestimated here: The lower a person's cultural leverage, the more restricted their ability to preserve the integrity of their social network and thus a degree of inner harmony. To illustrate with a historical example, a Black slave could not prevent the selling of her spouse or children: The deleterious effects of such an experience on the physical and mental health of African Americans have yet to be fully evaluated. In the model, we attribute to the factor of sustained harmonious contact a role equivalent to that of a *strange attractor* (in nonlinear dynamics), that is, it serves to control the effects of other variables, such as SES, stress, and transiency. The inability to maintain one's social network carries dire consequences. Generally speaking, Wilkinson (1999) has made the point that social isolation is perhaps one of the top two risk factors for population health. At an individual level, a stable personal relationship seems to affect longevity: It has been reported that divorced men have a shorter life expectancy than married men. The work of Francis and Meany (2002) has shown that maternal nurturing early in life has long-term consequences on progeny's behavior and health. But even short-term relationships may affect hormonal balance. Oxytocin, for example, is sensitive to social behavior geared toward empathy and bonding. Social reinforcement, or a lack of it, is known to lead to fluctuations in the level of forebrain serotonin.

Biological Factors Affecting Health

The INGAM model anchors its analysis of the relationship between biological factors and health to family history. Family health history includes not only medical conditions but also unique life experiences and the risk-taking behaviors of parents. The influence of family health can be tracked along three pathways. The main pathway may be genetic. But because genes

cannot tell the whole story, two other pathways, the epigenetic and the intrauterine, are perhaps equally important.

Genetic pathway—There is a direct link from family history to the personal genome of the offspring. Each parent contributes 50% of the chromosomes to their child. Any disease that affects the germline can be transmitted from one generation to the next through various modes of inheritance. Each child in a family has a 50% chance of inheriting an autosomal dominant disorder from a parent. In the case of a recessive marker, when both parents are carriers of the trait, the probability exists that some of their progeny will develop the disease. For instance, with sickle-cell anemia, if both parents in a family are carriers of the trait, each of their children has a 25% chance of developing the disease (Ashley-Koch, Yang, & Olney, 2000). A disease is often accompanied by mutations in one or more gene. With sickle-cell disease, a mutation occurs on the β -globin gene, whereby the 6th amino acid on the 17th nucleotide in the chain encodes for valine instead of glutamic acid (Geva, Clark, & Zhang, 2004).

The pattern and frequency of some mutations can be associated with biosocial factors. For instance, variations in genes that control the human leucocyte antigen complex (HLA-DQ) seem to be contributing to Type 1 diabetes. But, among European Americans, it is the DQ-A1-0201 allele that is implicated, while among African Americans it is the DQ-B1-0201 allele that carries significance (Dorman & Bunker, 2000). Polymorphisms that are relevant to drug metabolism can also be associated with biosocial identity. Depending on the speed of absorption, a particular drug may seem not to work with one patient while it creates dose-related side effects in another. According to Seashore (2004) “polymorphisms in the CYP cytochrome P-450 genes alter the metabolism of a variety of medications, including anti-coagulants, antihypertensives, and anti-arrhythmic drugs” (p. 183). Weinshilboum (2004) has added, regarding the gene CYP-2D6, that “the occurrence of multiple copies of this gene is relatively infrequent among Northern Europeans; in East African populations, the allele frequency can be as high as 29 percent” (p. 45).

Epigenetic pathway—The extent to which a mutation changes the function of proteins and thus gene expressions can somewhat be tempered. The mechanism involves gene regulation, that is, the process of selectively silencing or delaying the expression of a gene. In the INGAM model, gene regulation plays a role equivalent to that of a *strange attractor* (in nonlinear dynamics), that is, it sets the parameters for a number of processes including differentiation of tissues, maintenance of functions, antiviral defense, the timing of a change, and many other aspects of cell development. Gene regulation requires the action of double-stranded RNAs, which interfere with transcription (RNAi). “Most frequently, the RNAi mechanism involves either blocking the translation of specific messenger RNAs—posttranscriptional gene silencing,—or preventing transcription of specific regions of DNA into RNA—transcriptional gene silencing” (Schachter, 2007). This has broad relevance to cancer, liver disorders, and infectious diseases (Stevenson, 2004). To illustrate the interaction of a gene with another and the significance of gene regulation for health maintenance, consider the role of the chemokine CCR5 as part of the immune response: A 32 base-pair deletion in the gene for this chemokine receptor seems to offer protection against HIV infection (Altshuler, 2004).

Intrauterine pathway—Not all effects of family history are captured as part of the genetic mutation process. Some will be mediated by the conditions of gestation. Genes are sensitive to environmental variations, particularly in the womb and during the early stages of cell development (Encha-Razavi et al., 2004). While the baby is in the womb, antibodies from the mother do cross the placental barrier and flow into the blood circulation of the fetus. If there is incompatibility between the blood type of the mother and that of the fetus, difficulties may arise, which affect both the current and subsequent pregnancies. A pattern is thus created. According to Crider, Whitehead, and Buus (2005), “approximately 20% of women who deliver

preterm subsequently have another preterm with the same partner; changing partner reduces the risk by one-third” (p. 595). A more common situation is that of a perfectly healthy woman who experiences a difficult pregnancy, with consequences for the baby at birth. A woman with uncontrolled high blood pressure is at a much higher risk of experiencing preeclampsia (Casas et al., 2006). Maternal zinc deficiency has been linked to low birth weight, while maternal iodine deficiency usually results in a similar problem for the offspring (Mason, 2004), with consequences for the development of the thyroid gland. A maternal viral infection, if transmitted to the baby, may set the stage for mental illness. Indeed, according to Song and Leonard (2000), “raised titres to viruses such as measles, varicella, cytomegalovirus are detected in higher concentrations in schizophrenic patients compared to control” (p. 106).

Functional Interdependence of the Subsystems

Activities across the three subsystems described above are somewhat coordinated through a set of signals geared to long-term as well as short-term communication. We hypothesize that functional interdependence is brought about via a *multipolar neurobiological circuit* or conveyor belt, which involves neurotransmitters, neuropeptides and hormones, melanocortins, protein kinases, and transcription factors. At one end of the circuit, genes with their multiple DNA sequences carry signals as well as timing instructions for very long-term communication (Meyer et al., 1998). The time frame here is in years. At the other end of the circuit are the neurotransmitters, which transform psychosocial signals (Cole, 2008) and carry very short-term communications. The time frame here is in milliseconds. The actions of hormones and neuropeptides tend to be more sustained in time. Protein kinases and melanocortins carry the signals from cell to cell and from organ to organ. A protein kinase plays a somewhat unique role in the neurobiological circuit: It is an enzyme, which through a process of phosphorylation (addition of phosphate groups to proteins) can operate as a switch to be turned on or off; thus it can alter the cellular location of other proteins or the function of a gene, as it receives signals from the other hubs on the circuit.

We adopt the stance that no signal is ever emitted in isolation. The appearance of a signal at any one point of the neurobiological circuit generates a cascade effect, that is, the mobilization of inputs at all the other points. This would help explain why genes never seem to act independently, but simply create a predisposition, which may be triggered if and when a behavioral or other physiological factor comes into play. For instance, a mutation in *Factor V Leiden* can lead to complications of blood clotting and deep-vein thrombosis. But the likelihood of such an outcome increases when a woman with that genetic predisposition is on oral contraceptives (Khoury, McCabe, & McCabe, 2004).

Communication can be *initiated* at any point along the neurobiological circuit; that is what makes it multipolar. So we further contend that the origin of the signal makes a difference to the message. For instance, a communication sequence that begins with a neurotransmitter and ends with a change in a transcription factor, may not have the same implication as one that begins with a transcription factor and ends with a neurotransmitter turnover. That would help explain for instance the dual contribution of the neurotransmitter dopamine to Parkinson's disease and to aggressiveness (Ledoux, 2000), two vastly different phenomena on the surface.

Conclusion

We propose the INGAM model as a nonlinear, integrated approach to study the relationships between social ecology, the genome, and health outcomes. This is an attempt to operationalize a multifactorial approach to illness and health. To illustrate with an example from mental health, we can take the finding that stressful life events strongly correlate with major depressive disorder. But the full impact of this relationship seems to be amplified in the presence of a polymorphism in the 5-HTT gene (Caspi, Sugden, & Moffit, 2003). At the same time, one must

keep in mind that sustained harmonious contact (social support) not only moderates stress, it can also affect gene transcription factors such as GR-NF κ B for glucocorticoid receptors (Cole, 2008). Even a simple and common behavior such as sleep can modulate gene expression (Cirelli, 2005).

With regard to racial disparities, the INGAM model invites researchers to move beyond the simple inventory and description of health outcomes unfavorable to African Americans in comparison with Whites. It rather seeks to draw attention to the question: What is to be done in order to change these outcomes? Here are, briefly, three areas for a plan of action.

1. Certainly, there are health disparities that are determined by strictly social factors, such as socioeconomic disadvantage, disenfranchisement resulting from limited cultural leverage, and racism. Differential access to medical care is a prime example. When faced with end-stage renal disease, African Americans are less likely to get an organ transplant referral, while Whites are more likely to be placed on a waiting list for transplantation even before their dialysis begins (Callender & Miles, 2004). More than 45 million Americans, many of them African Americans, are without adequate health insurance. This situation must change, and the decision makers must be prodded into adopting the policies that can bring significant improvement in every area. But the problems cannot be tackled always from a distance and in broad strokes. We must get to “ground zero,” where contact occurs between patients and health care providers, to ensure that our resources are spent judiciously and in a targeted fashion. For instance, we need to obtain better and more proactive prenatal care. The rate of low birth weight in the African American community, even after adjusting for SES, is unacceptably high. We know that maternal nutrition, particularly zinc deficiency, can lead to low birth weight. Prenatal exposure to cytokines may set the conditions for obesity, a growing problem in the United States (Dahlgren, Nilsson, & Jennische, 2001). An immune insult to the expecting mother can carry to the offspring, affecting its catecholamine level, more specifically brain dopamine (Bakos et al., 2004), possibly compromising mental health in years to come. Early detection may help prevent the effects of all those problems.
2. Following a tenet of social ecology, the INGAM model builds on the centrality of habitat in relation to health status. What we want to further underscore here is that the impact of the environment on health may sometimes vary as a function of ethnicity. Therefore, an item on the social agenda must be the exercise of greater control over the environment in which we live. Specifically, African Americans need to be vigilant and steadfast in mobilizing against the target-marketing of certain toxic products to our community, because such products are likely to affect our health earlier and with more devastating effects. For instance, in a large study published recently, Haiman and other researchers at the University of Southern California (2006) reported that even light to moderate smoking tends to increase by 55% the odds for lung cancer among African Americans as compared with Whites. Findings such as these suggest that we do not yet have the full picture on the sensitivity of our immune system or on the rate at which we may metabolize certain chemical substances (Weinshilboum, 2004). In the meantime, we can ill-afford complacency toward certain behaviors and actions that may benefit some commercial sectors but are detrimental to our health and create or exacerbate racial disparities.
3. There are health problems prevalent in the African American community for which medical practice, in its current state, has no satisfactory response yet. Therefore, we have a vested interest in pushing the frontiers of medical research, including in the area of genomics. One example may suffice to illustrate the point. Sickle-cell anemia afflicts 1 in 700 African Americans. This is a condition in which red blood cells

become deoxygenated, change in viscosity, and thus lose their ability to move through small capillaries (Embury, 2004). We now know that this disruption is tied to a mutation on the β -globin gene, whereby valine replaces glutamic acid in the amino acid chain (Geva et al., 2004). Is there perhaps an epigenetic mechanism that would allow for the neutralization of this mutation? Is there another polymorphism that may signal an alternative pathway for cell viscosity? Are there environmental (nutritional) factors that may, if tactfully controlled, help with the adequate oxygenation of red blood cells? Answers to these questions would carry great practical significance.

Generally speaking, we have tried as much as possible, in constructing the INGAM model, to bring to light research evidence on which each pathway in the model is predicated. But we realize that some of the pathways only represent hypotheses that redirect some existing findings and call for a reevaluation of some favored conclusions. Such is the case with the relation between SES and health. Nevertheless, as presently configured, the model suggests a number of lines of investigation and areas in need of more focused basic research.

With regard to genomics, researchers need to better understand the mechanisms of gene regulation. Currently, much is known about gene mutations, and much effort is geared toward the development of pharmaceutical products targeting some of these mutations. Greater understanding of gene regulation would not only help better manage drug metabolism and side effects, it would also make clear how the organism autonomously engages in internal damage control, which is a key factor in disease prevention. The success of personalized medicine depends in no small measure on that understanding.

With regard to social ecology, more research is needed on the role of nutrition and nutrient imbalance, particularly in vulnerable populations. We have also put forth the concepts of cultural leverage and transiency as a dual complement, if not a radical alternative, to the traditional indicators of SES. Researchers may find those concepts useful for giving breath to their analysis of discrimination and/or institutional racism. Either concept also stands to cast in a new light the role of stress as a mediator between identity and health.

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Figure 1. INGAM Model: Identity Network, Genome, and Affect as Modulators of Health

TABLE 1
Comparative Profile of African Americans and European Americans Based on 15 Leading Causes of Death (Both Genders, All Age Groups, in the Year 2000)

Rank	Cause	African Americans			Whites		
		Percentage of Total	Rate per 100,000	Cause	Percentage of Total	Rate per 100,000	
1	Heart disease	27.1	219.6	Heart disease	30	278.8	
2	Malignant neoplasm	21.7	175.5	Malignant neoplasm	23.2	212.2	
3	Cerebrovascular disease	6.7	54.4	Cerebrovascular disease	7	63.9	
4	Accidents	4.3	34.8	Chronic lower respiratory problems	5.4	49.9	
5	Diabetes mellitus	4.2	34.1	Accidents	4	36.5	
6	Homicide	2.8	22.3	Influenza/Pneumonia	2.8	25.6	
7	HIV/AIDS	2.7	22.2	Diabetes mellitus	2.7	24.6	
8	Chronic lower respiratory problems	2.6	21.5	Alzheimer's disease	2.2	20.5	
9	Nephritis/nephrosis	2.4	19.6	Nephritis/Nephrosis	1.4	13.1	
10	Influenza/pneumonia	2.1	17	Suicide	1.3	11.7	
11	Septicemia	2.1	16.8	Septicemia	1.2	11	
12	Conditions from perinatal period	1.8	14.2	Liver disease	1.1	10.2	
13	Primary hypertension or renal disease	1.4	11	Parkinson's disease	0.7	6.6	
14	Liver disease	1	7.8	Pneumonitis	0.7	6.6	
15	Alzheimer's disease	1	7.7	Aortic aneurysm	0.7	6.3	
	All others	16.2	131.2	All others	15.5	142.2	

SOURCE: Centers for Disease Control and Prevention/National Center of Health Statistics, National Vital Statistics System, Table LCWK1 (2002).