BIODEMOGRAPHY

by

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PREAMBLE

Biodemography can be compared with a tree with two main branches, each with many smaller branches, and with deep historical roots, a tree that currently is relatively small but burgeoning rapidly. Although still a modest sub-field within demography, biodemography is arguably the fastest growing part of demography and the most innovative and stimulating. The two main branches today involve: (1) biological-demographic research directly related to human health, with emphasis on health surveys, a field of research that might be called biomedical demography (or "epidemography" because it is a cross between demography and epidemiology), and (2) research at the intersection of demography and biology (as opposed to biomedicine), an endeavor we will refer to as biological demography. The first branch is characterized by demographers engaging in collaborative research with epidemiologists. This is very important, for both fields and for deeper understanding of human health. Researchers in the second branch face an even bigger challenge. Demographic and epidemiological concepts and methods are fairly similar, whereas the underlying paradigms of demography and biology are less related.

Both of the two main branches of biodemography have many smaller branches. As in any innovative, rapidly-growing interdisciplinary field, these smaller branches form tangles and thickets. Consequently, it is difficult to present a coherent structure for the evolving research in biodemography. One way to proceed is to make use of the hierarchical ordering of knowledge within biology. This hierarchical ordering provides a basis for ordering the research subdivisions that range from the molecular and cellular to the ecological and evolutionary. This ordering of biodemography by levels is useful because, as the eminent physiologist George Bartholemew (Bartholomew 1964) noted over four decades ago: *"…each level [of biological integration] offers unique problems and insights, and …each level finds its explanations of mechanism in the*

levels below, and its significance in the levels above." For example, the results of studies on different APOE gene alleles shed important light on a molecular mechanisms for different risks of ischemic heart disease, Alzheimer's disease and other chronic conditions and thus provides information on a person's individual risk of these chronic diseases and, in turn, informs the design of population surveys and model construction for epidemiological forecasting (Ewbank 2004).

We used this organizational concept in Table 1 to summarize what we believe are the main disciplinary subareas of biodemographic research within each of three broad levels of biological organization—Level I (molecular to physiological), Level II (individual to kin), and Level III (population to evolutionary processes). Although several of the research categories in Table 1 are arbitrary and the range of research examples cited in each is incomplete, we believe that the information contained in this table captures the emerging scope and complexity of the field and highlights the considerable potential for scientific synergy through interdisciplinary research.

{Table 1 around here}

The subdisciplines listed within each of the three levels have the potential to be mutually informing both within and between categories and levels. There are also a number of instances where closely-related concepts were independently derived in population biology and demography. For example, the early work by Andrei Rogers on multiregional demography (Rogers 1984; Rogers 1985) is conceptually identical with recent work on meta-population analysis in conservation biology (Hastings and Harrison 1994). The studies involving 'geographic structure' in wild populations of animals (Roderick 1996) are similar to studies concerned with many of the same questions and the use many of the same genetic tools as those

in epidemiological demography (Ewbank 2000; Finch and Tanzi 1997; Finch et al. 2000; Wallace 1997; Wallace 2000). Although applied in much different contexts, at their roots the use of the concept of natural selection (Meagher and Futuyma 2001) has parallels with the concept of demographic selection (Vaupel et al. 1979) since both involve a winnowing process.

The remainder of this chapter is structured as follows. We begin with an extended discussion of the branch of biodemography that we call biological demography. Then we turn to a shorter description of the other main branch, the branch we call biomedical demography. That is, the bulk of this chapter focuses on biological demography. The biomedical branch is at present at least as prominent as the biological branch, with at least as many demographers actively involved. And the biomedical branch is certainly pathbreaking, with substantial results to date and much promise. In our section on it, we list some of the key researchers and main publications. We decided, however, to emphasize biological demography because the concepts and methods of biomedical demography are quite accessible to demographers whereas the concepts and methods of biological demography are much more foreign and difficult to understand. In particular, we believe that understanding biological thinking in demography requires appreciation of a set of biological-demographic principles. A major portion of the chapter is devoted to an exposition of these principles and the more general concept of why it is useful and important to think in terms of such principles.

BIOLOGICAL DEMOGRAPHY

Conceptual Framework

Biological demography is an emerging interdisciplinary science concerned with identifying a universal set of population principles, integrating biological concepts into demographic approaches, and bringing demographic methods to bear on population problems in

different biological disciplines. Whereas biomedical demography brings survey techniques, biomedical information, modeling strategies and statistical methods to bear on questions about the health of different *human populations*, biological demography brings experimental paradigms, model systems, evolutionary perspectives and comparative techniques to bear on questions about the demographic characteristics of different *species*. Biomedical demographers might ask questions about the shape of the trajectory of human mortality at advanced ages. In contrast, biological demographers will ask the more general question of whether the slowing of mortality at advanced ages is a universal life table characteristic of species as diverse as nematodes, fruit flies, mice, and humans. Biological demography not only situates the population traits of humans within the broader demographic characteristics of all living organisms but it also provides a scientific framework for asking basic questions that differ from but are complementary to conventional demography.

Because of the range of the sub-disciplines within biology and of the sub-specialties within demography, the term 'biological demography' does not fully reflect the diversity of its main intellectual lineages including gerontology, population biology, and demography (Hauser and Duncan 1959a), the complexity of its deep historical roots (Malthus 1798; Pearl 1922), or the scope of the questions that are commonly addressed by biological demographers themselves (Carey and Tuljapurkar 2003; Vaupel et al. 1998; Wachter and Finch 1997). Although biological-demographic researchers use mathematical and statistical modeling techniques similar to those used in classical demography, they also use experimental methods to address questions about the nature of mortality and fertility, development and aging in such model organisms as fruit flies and rodents. Thus unlike most research in classical demography, biological-

demographic research exploits the hierarchical ordering of knowledge that unites and drives the biological sciences.

Biological demography embraces all the research at the intersection of demography and biology. It hence includes studies of fertility, migration and mortality. To date, however, the main emphasis has been on studies of survival and longevity, with some emerging research on fertility and on the links between fertility and mortality. Whereas the traditional paradigm around which biological gerontology is framed is concerned with questions at molecular, cellular, and/or physiological levels, the biological-demographic paradigm of aging integrates research at the organismal level—the quintessence of biological relevance because all discoveries at lower levels of biological organization concerning aging must ultimately be tested at the level of the whole organism. And unlike traditional research in both classical demography and the biology of aging, biological demography draws from population biology and thus emphasizes evolutionary and ecological concepts, life history theory and comparative methods. This multidisciplinary synthesis represents a unique research paradigm that is concerned with both proximate questions (e.g., those concerned with the *mechanisms* of aging) as well as with ultimate ones (e.g., those concerned the evolutionary and ecological *function* of a particular life span). Thus biological-demographic research embraces many questions about both aging and life span that do not fall within the bounds of either traditional demography or gerontology.

Contribution to Mainstream Demography

Biological demography can strengthen traditional demography in at least three ways. *First*, the concepts, principles, and theories developed in biological demography can enhance coherence and the development of a higher unity of order and process. This higher unity cannot occur without viewing the human life course in the context of other components or processes.

Biological demography has the potential for integrating biology into the pedagogical framework of classical demography in much the same way as basic biology is integrated into biomedicine. The focus on humans is retained but the epistemological foundations are strengthened, the biological scope is expanded, and the demographic perspectives are broadened.

Second, results from experimental biological demography will provide better explanations for the life table patterns observed in human populations that are not evident in the absence of broader biological concepts. For example, biological-demographic principles link senescence and sexual reproduction. The principles suggest explanations of sex differentials in life expectancies, why older individuals may grow older more slowly, whether life span limits exist, whether post-reproductive life is common or rare, the relationship between sociality and life span, and if and how post-reproductive life spans in other species increase fitness.

Third, the biological-demographic principles will provide a more secure foundation for making predictions about the trajectory of mortality at older ages, the nature of life span limits (or lack thereof), and the magnitude and sign of the gender gap. In general, every discipline including demography is faced with the perennial struggle to define and renew itself and to ensure its relevance in an ever-changing world. Like other social sciences, demography is slowly coming to terms with important truths that the biological sciences have proved beyond any doubt—that all aspects of humans—mind, behavior, body—are products of biological evolution (Foster 2000). It follows that this program in particular but biological demography in general will help demography maintain a robust, energetic, and creative presence in modern science.

As Preston (Preston 1990) points out, instead of demographers asking why life expectancy at birth for the world as a whole has doubled in this century, demographers might ask the more biological question regarding why no one has ever been recorded living past age 122.

Instead of asking why childbearing is increasingly delayed in the United States, demographers might ask why the reproductive life span for women is essentially confined to ages 15 to 50. Or instead of asking why the gender gap favors females by 4 to 10 years in developed countries, demographers might ask whether a female longevity advantage is present in the majority of non-human species.

HISTORICAL OVERVIEW

Early History

Demography has multiple points of contact with biology, as well as mathematics, statistics, the social sciences, and policy analysis. Although population biology and demography share common ancestors in both T. R. Malthus {Malthus, 1798 #277} (i.e. populations grow exponentially but resources do not) and Charles Darwin (Darwin 1859) (i.e. selection on birth and death rates resulting from struggle for existence), the more contemporary biology-demography interface served as the research foundation of two distinguished demographers in the early decades of the twentieth century—Alfred J. Lotka (1880-1949) and Raymond Pearl (1879-1940). Lotka developed concepts and methods that are still of fundamental importance in biological demography; his two most significant books are *Elements of Physical Biology* (Lotka 1924) and *Theorie Analytique des Associations Biologiques* (Lotka 1934). Pearl pioneered biological-demographic research on several species, including flatworms, the aquatic plant *Ceratophyllum demersum*, the fruit fly *Drosophila melanogaster*, and humans (Pearl 1924; Pearl 1925). He founded two major journals, the *Quarterly Journal of Biology* and *Human Biology* and helped found both the Population Association of America (PAA) and the International Union for the Scientific Investigation of Population Problems (which later became IUSSP—the International Union for Scientific Study of Population). Following the pioneering work of Lotka

and Pearl in the 1920s and 1930s there was, until the 1970s, little interest among demographers in integrating biology into any part of the discipline. There were a few chapter entries on population studies in such crosscutting disciplines such as demography and ecology (Frank 1959), demography and anthropology (Spuhler 1959) and genetics and demography (Kallmann and Rainer 1959) in the seminal book *The Study of Populations* by Hauser and Duncan (Hauser and Duncan 1959b). These and other similar chapters served more as illustrations of how demographic methods were used by different disciplines than as sources of knowledge for demography.

Convergence of Ideas

In the early 1970s a group of population biologists and demographers, including Nathan Keyfitz, launched the journal *Theoretical Population Biology* (TPB). The journal was intended to be a forum for interdisciplinary discussion of "the theoretical aspects of the biology of populations, particularly in the areas of ecology, genetics, demography, and epidemiology." This description is still used by the publisher to describe the journal, but the publisher describes the audience of the journal as "population biologists, ecologists, evolutionary ecologists", with no mention of demographers (or epidemiologists). Some demographers over the years have published articles in TPB, but the journal, which has thrived and is now published 8 times per year, has indeed become dominated by population biologists and evolutionary ecologists. As the more mathematical aspects of biological demography develop, TPB may finally be able to attain its original goal.

In the late 1970s IUSSP members expressed concern that demography was at risk of isolating itself and becoming more a technique than a science. Demographer Nathan Keyfitz lamented (Keyfitz 1984a) that "…*demography has withdrawn from its borders and left a no*

man's land which other disciplines have infiltrated." Hence in 1981 a workshop titled *Population and Biology* was organized at the Harvard University Center for Population Studies (Keyfitz 1984b) to explore the possible impact of biological 'laws' on social science (Jacquard 1984; Lewontin 1984; Wilson 1984), the selective effects of marriage and fertility (Leridon 1984), the autoregulating mechanisms in human populations (Livi-Bacci 1984), and the concepts of morbidity and mortality (Cohen 1984). That no notable papers or concepts emerged from this meeting between biologists and demographers, many of whom were among the most prominent scientists in their respective fields, was itself significant—the good intensions of top scientists are not enough to integrate two fields with fundamentally different disciplinary histories, professional cultures, and epistemological frameworks. To make progress it is imperative that a clear set of important (and ultimately fundable) questions be laid out that lie at the disciplinary interface. This is particularly importance for integrating disciplines with disparate historical roots such as demography with its roots in the social and analytical sciences versus biology with its roots in the natural and experimental sciences.

In the mid-1980s two separate meetings were organized that brought scientists together to address more circumscribed and focused questions that lie at the interface between biology and demography. The first workshop that brought biologists and demographers together during this period was organized by Sheila Ryan Johannson and Kenneth Wachter at the University of California, Berkeley in 1987, supported by National Institute on Aging (NIA), and titled "*Upper Limits to Human Life Span*". Although there were no publications and/or proceedings from this workshop, it was important historically because it was the first meeting to bring biologists and demographers together to focus expressly on a circumscribed topic of great importance to demographers, biologists and policy makers—aging and longevity. This workshop set the stage

for virtually all of the subsequent developments in the biological demography of longevity and aging.

The second workshop during the late 1980s that helped to frame biological demography was organized in 1988 at the University of Michigan by Julian Adams, Albert Hermalin, David Lam and Peter Smouse titled *Convergent Issues in Genetics and Demography* (Adams 1990). This edited volume included sections on the use of historical information including pedigree and genealogical data in genetics and demography, on the treatment and analysis of variation in the fields of genetics and demography, on epidemiology as common ground for the convergence of demography and genetics, and on issues in genetics and demography that have attracted attention of scientists in both fields such as two-sex models, minimum viable population size and sources of variation in vital rates. This workshop on genetics and demography was significant because it revealed the importance of organizing research at the interface between biology and demography around a circumscribed topic, in this case genetics.

Recent Coalescence

The Berkeley and Ann Arbor workshops set the conceptual stage for the organization of a cluster of three highly-successful workshops held between 1996 and 2001. The first of these was a workshop on *Biodemography of Longevity* that was organized and chaired by Ronald Lee of the Committee on Population of the U.S. National Research Council and held in Washington DC in April 1996. This meeting is was one of the seminal developments in biological demography because of the new insights and perspectives that emerged on the nature of aging and life span from the interchange of demographic and biological ideas. The workshop led to the book "*Between Zeus and the Salmon: The Biodemography of Longevity"* edited by Kenneth Wachter and Caleb Finch (Wachter and Finch 1997): this volume includes papers on the empirical

demography of survival, evolutionary theory and senescence, the elderly in nature, postreproduction, the human life course, and intergenerational relations, the potential of population surveys in genetic studies, and synthetic views on the plasticity of human aging and life span.

The second workshop, organized and chaired by Kenneth Wachter and Rodolfo Bulatao, focused on fertility and was designed to complement the workshop on the biological demography of longevity. Like the others preceding it, this workshop brought together demographers, evolutionary biologists, geneticists and biologists to consider questions at the interface between the social sciences and the life science. Topics included in the resulting volume (Wachter and Bulato 2003) included the biological demography of fertility and family formation, genetic and ecological influences on fertility, education, fertility and heritability, mating patterns, energetics and sociality of human reproduction.

The most recent workshop concerned with biological demography was organized by James Carey and Shripad Tuljapurkar and titled "*Life span: Evolutionary, ecological, and demographic perspectives*": it was held in 2001 on the Greek Island of Santorini (Carey and Tuljapurkar 2003). This workshop was a follow-up to the earlier one on biological demography but with a greater emphasis on life span rather than aging, per se. The edited volume from this workshop included papers on conceptual and/or theoretical perspectives on life span and its evolution, ecological and life history correlates, and genetic and population studies of life span in both non-human species and in humans.

At the beginning of the twenty-first century biological demography is reemerging as a locus of cutting edge demographic research. It is clearly accepted that fertility, mortality, morbidity, and other processes of profound interest to demographers have a basic biological

component. Moreover, biology is fundamentally a population science and there is growing recognition that biological studies can benefit greatly from demographic concepts and methods. From a biologist's perspective, biological demography envelops demography because it embraces research pertaining to: any nonhuman species; populations of genotypes; and biological measurements related to age, health, physical functioning, and fertility. Within this vast territory, several research foci are noteworthy and are briefly described in the next section.

GENERAL BIOLOGICAL DEMOGRAPHIC PRINCIPLES

Inasmuch as scientific principles and hard data are bound together in close etiological and epistemological relationships, the usefulness of the store of data from biological demography is enhanced through the synthesis of these data using a dialectic combination of demographic and biological concepts. Our objective in this section is to summarize a number of general principles that have been identified from recent research in biological and comparative demography (Carey 2003b; Carey and Judge 2001).

Conventional demography, defined by Pressat (Pressat 1985) as *"the study of populations and the processes that shape them"*, is a science dependent for its data on observation and recording of events occurring in the external world rather than on experiments under controlled conditions. One of the overriding constraints of any of the observational social sciences such as demography and sociology was referred to by Hauser and Duncan (Hauser and Duncan 1959a) as "the problem of historicism"—the question of the extent to which generalizations drawn from human data localized in time and space can lead to general principles rather than simply to descriptions of situations unique to a particular time and location. This constraint preempts the use of any human data alone as a source for the derivation of the most basic principles.

Principles of Senescence

Timiras (Timiras 1994) notes that despite some minor interpretative differences the terms aging and senescence are often used interchangeably—aging refers to the process of growing old regardless of chronologic age whereas senescence is a process restricted to the state of old age characteristic of the late years of an organism's life span. Senescence in this context is defined as *"the deteriorative process characterized by increased vulnerability, functional impairment, and probability of death with advancing age"* (Timiras 1994). In this section we describe two principles of senescence that are fundamental to biological demography because they provide the biological, evolutionary, and conceptual foundation for its constituent disciplines—whereas demography is concerned with the determinants of probabilities of death, biology is concerned with the determinants of vulnerability.

Natural selection shapes senescence rate

All systems, from the simplest kind of equipment to the most complicated species of life, senescence, at least in their component parts. Whether or not the entity as a whole suffers senescence, however, depends on the balance between the forces of wear and tear, on the one hand, and the counterbalancing forces of repair and rejuvenation, on the other. For living organisms, this balance is determined by natural selection, by Darwinian evolution.

Evolutionary models of life-history characteristics in general and of senescence in particular fall into two types (Partridge and Barton 1993), optimization models and non-adaptive age-specific mutation models. In optimization models the forces of evolution are assumed to yield the best-possible design of a species' life history, the design that maximizes Darwinian fitness. Williams (Williams 1957) proposed an optimization model of senescence, the so-called antagonistic-pleiotropy model. The basic idea is that some genes have a favorable or unfavorable

effect on fertility or survival at younger ages but the opposite effect on mortality at older ages. A small positive (or negative) effect at younger ages may be more important than a large opposite effect at older ages if few individuals survive to these ages and if their reproduction is low. Williams' model is often formulated in terms of mutations that have a positive effect at some particular age and a negative effect at some other age (Charlesworth 1994). Williams' idea, however, is more general. It is simply an example of the kind of thinking about trade-offs that underlies all optimization modeling. Williams thought that his model implied senescence and he did not consider the logical possibility that such an optimization model might lead to negative senescence, i.e., to the decline in mortality with age (Vaupel et al. 2004). The "disposable soma" model (Kirkwood 1992; Kirkwood and Rose 1991) is a related example of this kind of thinking applied to senescence.

In the second class of models evolutionary forces act in a non-adaptive way, as follows. Evolution acts on randomly occurring mutations. Some of these mutations may have age-specific effects. In particular, some mutations may only be harmful at older ages. There is little selective pressure to remove such mutations from the population because the individuals who have them have produced most of their offspring before they have reached old age. Hence, such mutations tend to accumulate, resulting in senescence. Charlesworth (Charlesworth 1994) provides a general discussion of mutation-selection balance, i.e., of models of the opposing forces of deleterious mutation and subsequent Darwinian selection. Hamilton (Hamilton 1966) developed an influential mutation-accumulation model of senescence.

All sexual organisms senesce

Hamilton's mutation accumulation model led him to conclude that senescence "cannot be avoided by any conceivable organism" and that "senescence is an inevitable outcome of

evolution". This view, combined with arguments made by Weissman in the 1880s and 1890s about the senescence of somatic cells and the immortality of germ cells, was developed by Bell (Bell 1988), who postulated a deep connection between the two invariants of life—birth and death—by demonstrating that protozoan lineages senesce as the result of an accumulated load of mutations. This senescence can be arrested by recombination of micronuclear DNA with that of another protozoa through conjugation. Conjugation (sex) results in new DNA and in the apoptotic-like destruction of old operational DNA in the macronucleus. Thus, rejuvenation in the replicative DNA and senescence of operational DNA is promoted by sexual reproduction. When this line of thinking is extended to multicellular organisms, sex and somatic senescence can be inextricably linked (Clark 1996). In multicellular, sexually reproducing organisms, the function of somatic cells (i.e. all cells constituting the individual besides the germ cells) is to promote the survival and function of the replicative DNA—the germ cells (Clark 1996). Prior to bacteria, the *somatic* DNA was the *germ line* DNA; prior to multicellular animals, the *somatic cell* was the *germ cell*. Like the macronuclei in the paramecia, the somatic cells senesce and die as a function of their mitotic task of ensuring the survival and development of the germ cells. The advent of sex in reproduction allowed exogenous repair of replicative DNA (Bell 1988) while in multicellular organisms the replication errors of somatic growth and maintenance are segregated from that DNA passed on to daughter cells and are discarded at the end of each generation. Senescence, according to Bell and Clark, is built into the life history of all sexually reproducing organisms. The death rate can be altered by modifying senescence but death itself can never be eliminated. This evolutionary argument concerning senescence as one of the fundamental canons in the emergence of all sexually-reproducing organisms.

Recently, however, the canon has been questioned. There is a deep inconsistency between Hamilton's view that senescence is inevitable even "in the farthest reaches of almost any bizarre universe" and the Weissman-Bell-Clark emphasis on senescence in sexually-reproducing species. In plants there is no distinction between the soma and the germ line, but at least for some plants mortality rises with age. Single-celled organisms that do not sexually reproduce certainly tend to have short lives: they can hardly be termed immortal except in the sense that the species survives. Furthermore, fundamental objections have been raised regarding Hamilton's model and resulting conclusions (Lee 2003; Vaupel et al. 2004). It seems clear that the component parts of any individual suffer wear and tear, but, as discussed above, under some circumstances the organism as a whole can experience constant or even declining mortality if the damaged parts can be repaired or discarded and replaced. Hence the assertion that all (sexual) organisms suffer senescence is no longer the truism it was once deemed to be. Research on this issue is one of the most exciting current topics in biological demography.

Principles of Mortality

The single most important function of the life table is age-specific mortality—the fraction of individuals alive at age x that die prior to age x+1. There are at least three reasons that this function is more important than, for example, cohort survival or life expectancy (Carey 2003b): (1) Death is an event constituting a change of stage from living to dead whereas survival is a continuation of the current state. Life table parameters are based on probabilities of measurable events rather than “non-events” like survival. This is important because death can be disaggregated by cause whereas survival cannot; (2) Age-specific mortality is algebraically independent of events at all other ages and thus changes in age patterns can often be traced to underlying physiological and/or behavioral changes at the level of the individual. With the

exception of period survival, this is not true for the other life table parameters; and (3) several different mathematical models of mortality e.g. (Gompertz 1825) have been developed that provide simple and concise means for expressing the life table properties of cohorts with a few parameters. In the following section we describe mortality concepts that we believe are both general and relevant to understanding mortality in humans.

Mortality decelerates at advanced ages

Slowing or deceleration of mortality at older ages has been observed in every large- scale life-table study on insects (e.g. *Drosophila*, houseflies, medflies, and bruchiid beetles) with similar patterns are observed in human populations (Carey 2003b). There are three reasons why this general principle is important (Carey et al. 1992):(1) it provides a conceptual and empirical point of departure from the Gompertz model of ever increasing, age-specific mortality; (2) it forces demographers and gerontologists to rethink the idea that senescence can be operationally defined and measured by the increase in mortality rates with age; and (3) it suggests that there is no definite life span limit.

Mortality is sex-specific

The prevailing wisdom in gerontology is that the female advantage in life expectancy is a universal law of nature. Carey and co-workers (Carey et al. 1995) tested whether a female longevity advantage exists for the medfly and discovered that the answer was not straightforward—males exhibited a higher life expectancy at eclosion, but females were 4 times more likely than males to be the last to die. They concluded that there were at least three reasons why it is impossible to state unequivocally that either males or females are “longer-lived” (Carey et al. 1995). First, longevity can be characterized in different ways (e.g., life expectancy at eclosion [day 0], life expectancy at day 30, age when 90% of the original cohort is dead [life

endurancy], maximal life span, etc.); one measure of longevity often favored one sex, whereas another measure favored the other sex. Second, there is considerable variation among cohorts for a given longevity measure. For example, neither male nor female longevity was greater in all of the cages regardless of the measure used. And finally, relative longevity for the two sexes was conditional on the environment in which they were maintained or the treatment to which they were subjected. Expectation of life for males and females was similar if flies were maintained in solitary confinement but favored males if the flies were maintained in grouped cages. The overall conclusion was that sex-specific mortality responses and, in turn, male–female life expectancy differences cannot be predicted a priori; and that a female-longevity advantage is not universal across species.

Mortality trajectories are facultative

The term "facultative" is used in biology to describe life history traits that have alternative conditions that often vary with environmental conditions. For example, clutch size in some birds, diapause in insects and diet selection in many animals are all considered facultative. we suggest that the term also applies to mortality patterns in the medfly and most other species because there exists no unique pattern—the specific trajectories frequently depend on the environmental conditions. One of the most compelling findings emerging from the collection of life table studies on the medfly, and one that was not evident even after the first large scale study was completed, is that the female mortality patterns are extraordinarily plastic. The reason this elasticity was not evident from the first series of studies is because none involved manipulations that altered the physiology and/or behavior of the flies. It is now apparent that manipulations that affect components of a fly's life history, such as irradiation, diet or mating, have a profound effect on the trajectory of mortality in females and less of an effect on male trajectories.

Selection shapes mortality trajectories

The concept of subgroups endowed with different levels of frailty is known as *demographic heterogeneity*, and the winnowing process as the cohort ages is referred to as *demographic selection* (Vaupel et al. 1979). As populations age, they become more selected because groups with higher death rates die out in greater numbers than those with lower death rates, thereby transforming the population into one consisting mostly of individuals with low death rates (Vaupel et al. 1979). The actuarial consequence of cohorts consisting of subsets, each of which possesses a different level of frailty, is that the mortality trajectory of the whole may depart substantially from Gompertz rates even though each of the subgroups displays Gompertz mortality rates. Vaupel and Carey (Vaupel and Carey 1993) fitted observed *C. capitata* mortality patterns with mixtures of increasing Gompertz curves and demonstrated that twelve subgroups were sufficient to capture the observed pattern of medfly mortality using a range of frailty values and initial proportions of subgroups. Demographic selection winnows the frail and leaves the robust and, thus, shapes the mortality trajectory as cohorts age.

Principles of Longevity

Longevity refers to the period between birth and death of an individual. It is operationalized in several different ways including: *expectation of life at birth*—the average number of years (days, weeks, etc) that a newborn will live, *median life span*—the age at which half of an initial cohort is dead (or alive); *life endurancy*—the age at which 90% of the original cohort is dead, and *record life span*—the age at which the longest-lived, observed individual died. As a life history trait longevity co-varies with other traits including body size, brain size, ability to fly, armored animals or with subterranean habits, and with sociality (Sacher 1978).

Longevity is adaptive

In evolutionary biology an "adaptation" is a characteristic of organisms whose properties are the result of selection in a particular functional context. Just like the different bird beaks are adaptations for exploiting different niches that must be balanced with the other traits such as body size and flight propensity, the longevity of an animal is also an adaptation that must be balanced with other traits, particularly with reproduction. The variations in the relationship between reproduction and longevity can only make sense when placed within the context of such factors as demographics, duration of the infantile period, number of young, and the species' ecological niche—the organism's overall life history strategy. Indeed, the longevity potential of a species is not an arbitrary or random outcome of evolutionary forces but rather an adaptive one that must fit into the broader life history of the species.

Longevity is positively correlated with body size between orders (e.g. the smaller rodents are shorter lived than the larger primates) though not necessarily within orders (e.g. longevity not correlated with body size in the seals and walruses (pinnipeds) or in the small bats) (Carey and Judge 2000). Longevity is also positively correlated with certain unique traits including flight ability (birds and bats), possession of armor (turtles; armadillos) and subterranean lifestyle (moles; mole rats). Analysis of the database revealed that life spans differ by a factor of over 50 in mammals, reptiles, amphibians and fish and by over 15-fold in birds. It also provided important biological and evolutionary context for human longevity—primates are long-lived mammals, great apes (gorillas; chimpanzees) are long-lived primates, and humans are long-lived great apes. Indeed, the analysis revealed that human longevity exceeds nearly all other species both relatively and absolutely. This finding is important because it suggests that extended

longevity should be considered along with features such as large brain, bipedalism and language as a key trait of our species.

Life span is indeterminate

Maximal length of life remains as one of the most compelling concepts in demography and gerontology. The validity of this concept is viewed by many as self-evident because different species exhibit different life expectancies; all individuals eventually die before the age of infinity; and, therefore, each species must possess unique and finite maximal ages. Kannisto (Kannisto 1991; Kannisto 1996) noted that the problem with this idea is that our knowledge of the nature of mortality makes it difficult to accept the notion that there is a single age that some individuals may reach but that none has any chance of surviving. He views the only valid alternative as the existence of an asymptote to which the probability of dying tends and that may or may not be near 100%. Manton and Stallard (Manton and Stallard 1984) noted that declines in the age specific rates of increase of mortality for male and female cohorts in the United States are inconsistent with a fixed life span limit. Wilmoth and Lundström (Wilmoth and Lundstrom 1996) state "…we have established the important empirical fact that the upper limits of the human age distribution has been rising steadily during the past century or more and shows no sign thus far of possessing a fixed upper bound." In general, we can conclude from our studies that it is possible to estimate medfly life expectancy, but these flies, and most likely other species as well, do not appear to have a characteristic life span. The concept of an *indeterminate* life span implied by the medfly data is fundamentally different from the concept of a *limitless* life span.

Reproduction is a fundamental longevity determinant

Most organisms, from yeast and plants to invertebrates, birds and mammals, suspend reproduction during periods unfavorable for reproduction by entering a different physiological mode. Such waiting strategies for prolonging survival while maintaining reproductive potential have been extensively documented in the physiological, ecological and natural history literature. For example, when food is scarce yeast enter a stationary phase, tardigrads form tuns, nematodes go into a dauer stage, mollusks and earthworms undergo a quiescence, fruit flies experience a reproductive diapause, long-lived queens in ants and wasps hibernate, some fish reabsorb their ovaries, amphibians and reptiles aestivate, mice retard their ovariole depletion, some birds (hummingbirds and swifts) become torpid, and plants suspend their physiological and reproductive activities. Recent research on medfly aging (Carey 2003b) revealed that female medflies may experience two physiological modes of aging with different demographic schedules of fertility and survival. These include a waiting mode in which both mortality and reproduction are low, and a reproductive mode in which mortality is low at the onset of egg laying but accelerates as eggs are laid. Medflies that switch from waiting to reproductive mode due to a change in diet (from sugar to full protein diet) survive longer than those kept in either mode exclusively. The switch from waiting mode to reproductive mode initiates egg laying and reduces the level of mortality below current rates but increases the rate of aging. Understand this relationship between longevity and reproduction in medflies is important because it links the reproductive fate of individuals with environmental conditions and points towards important causal mechanisms that may be related to and mediated by the rate of ovarian depletion and/or gonadal activity(Carey 2003b).

The heritability of individual life span is modest

Life span heritability is defined as the proportion of the variance among individual ages of death that is attributable to differences in genotype. Contrary to popular myth parental age of death appears to have minimal prognostic significance for offspring longevity (McGue et al. 1993). Finch and Tanzi (Finch and Tanzi 1997) noted that the heritability of life span accounts for less than 35% of its variance in short-lived invertebrates (nematode; fruit flies), mice and humans. Although McGue and co-workders (McGue et al. 1993) found evidence for genetic influences, environmental factors clearly accounted for a majority of variance in age at death. For example, these researchers reported that the average age difference at death for twins was 14.1 and 18.5 years for identical (monozygotic) and fraternal (dizygotic) twins, respectively, and 19.2 years for two randomly-chosen individuals. The study by Herskind and co-workers (Herskind et al. 1996)followed more than 2800 twin-pairs with known zygosity from birth to death. This study showed that about 25% of the variation in life span in this population could be attributed to genetic factors. Generally, traits that are most essential to the survival of an organism including survival itself, show little heritability due to strength of selection and fixation.

Biological-demographic Principles and the Human Primate

Most of the biological-demographic principles concerning senescence, mortality and longevity presented in the previous section are general and thus apply to a large number of species. There are also actuarial characteristics in all species including humans that are specific to that species or a narrow group to which a species belongs. Such species level characteristics are superimposed on the more general patterns. For example, the general mortality patterns in humans includes a decline after infancy, increases through the reproductive life span (the overall

U-shaped trajectory), and a sex differential. However, the specific level pertains to details of the mortality experience unique to humans including the actual probabilities of death by age, inflection points of age-specific mortality, the cause-specific probabilities of death, and the age-specific pattern of the sex differential. The observed actuarial patterns are a combination of the evolutionary components of the trajectory (which will be common to a large number of species with overlapping life history characteristics) and the proximate age and sex-specific factors contributing to mortality and survival under certain conditions.

A variety of life history traits largely unique to humans are widely documented in anthropology and human biology texts. These include bipedalism, large brains, complex language, tool use, and a prolonged juvenile period. However, the extraordinary absolute longevity of humans, as well as longevity relative to body size, is a life history trait that is not fully recognized and appreciated. The purpose of this section is to identify and describe 3 biological-demographic principles that link our primate evolutionary past with modern human longevity. A substantial part of this section is based on results presented in (Judge and Carey 2000).

Body and brain size predict extended human longevity

As discussed above, most species, including humans, do not have a definite maximum life span. The oldest age reached in a a population depends on the size of the population and on environmental conditions. If, however, mortality rises steeply with age, as is the case for humans, primates more generally, and most mammals, and if population sizes are roughly comparable--on the order, say, of thousands or millions--then as a crude but useful approximation it is possible to characterize the maximum likely lifespan of individuals in such a

population as, say, "50-55 years years" or "about 30 years" (Vaupel 2003). The following discussion uses this notion of approximate (maximum) life span.

Brain size is correlated with both body size and life span in mammals as a whole and within the Primate order. Relative brain size and relative life span (residual brain and life span after controlling for body mass) are highly correlated (n =72 species). Judge and Carey (Judge and Carey 2000) examined longevity records for 133 species of primates relative to adult female body size and adult brain size and placed human life span in context relative to extant primates, and estimates for early (extinct) hominids. The great apes have absolutely long lives that slightly exceed the life span predicted by body and brain size. However, the closest relatives of humans (gorillas and chimpanzees) are exceeded in their positive deviation from the expected by 5 other Old World primate genera. No Old World non-human genus approaches the positive deviation from expected life span demonstrated by New World monkeys of the genus *Cebus* (i.e. Capuchin monkeys). *Cebus* exhibit life spans that rival those of chimpanzees even though chimps are roughly 15 times larger. The 25 year life span predicted by *Cebus* body and brain size is much exceeded by the 45-50 year life spans actually observed.

Long-lived monkeys have life spans proportional to human centenarians

Centenarian humans are not out of the scope of primate longevity, especially given the large numbers of human observations (i.e. high numbers increase the probability of sampling the extreme right tail of the distribution). *Cebus* monkeys exhibit *relative* life span potentials similar to humans and are convergent in traits such as a relatively large brain, generalized ability to exploit a wide range of ecological niches over a broad geographical distribution, fruit-based omnivorous diet, and polygynous mating systems (Judge and Carey 2000). While *Cebus* are female philopatric (females remain in their natal groups while males disperse), whether human

ancestors were male or female philopatric is unresolved. If human ancestors had the potential for 72-90 year life spans for 1-2 million years, one might wonder why prolonging life span to 100 years under modern conditions of ecological release has not been easier?

Post-reproduction expected from primate patterns

Hammer and Foley (Hammer and Foley 1996) incorporated body and raw brain volume estimates from fossil crania to predict early hominid longevity using a multivariate OLS regression of the log body weight and brain volume. Estimates based on regressions of anthropoid primate subfamilies or limited to extant apes indicate a major increase in longevity between *H. habilis* (52-56 years) to *H. erectus (*60-63 years) occurring roughly 1.7 to 2 million years ago. Their predicted life span for small-bodied *H. sapiens* is 66-72 years. From a catarrhine (Old World monkeys and apes) comparison group, our prediction is 91 years when contemporary human data are excluded from the predictive equation. For early hominids to live as long or longer than predicted was probably extremely rare; the important point is that the basic Old World primate design resulted in an organism with the potential to survive long beyond a contemporary mother's ability to give birth. Notably, Hammer and Foley's predicted life span of *Homo habilis* exceeds the age of menopause in extant women by 7 to 11 years and that of *H. erectus* exceeds menopause by 15-18 years. This suggests that post-menopausal survival is not an artifact of modern life style but may have originated between 1 and 2 million years ago coincident with the radiation of hominids out of Africa.

Williams (Williams 1957) first suggested that menopause may be the evolutionary result of a human life history that requires extended maternal care of offspring. Diamond (Diamond 1992) noted that menopause probably resulted from two distinctly human characteristics: (1) the exceptional danger that childbirth poses to mothers; and (2) the danger that a mother's death

poses to her offspring. Perinatal mortality increases with maternal age and the death of an older mother endangers not only her current infant but those past infants still dependent on her for food, protection, and other forms of care. However, more recently Hawkes and co-workers (Hawkes et al. 1998) have argued that it is post-reproductive longevity that has evolved rather than an early cessation of female reproduction; the reproductive spans of human and other ape females are not appreciably different. Rather, kin selection for older relatives subsidizing the reproduction of younger female kin may have been a primary mechanism extending human life span (the “grandmother hypothesis”). This subsidization also allowed humans a later age at maturity and, as a result, a longer period of time for growth and learning.

AN EMERGING BIOLOGICAL-DEMOGRAPHIC PARADIGM

The view of many demographers towards biology is similar to the view of many sociologists who believe that "biology" and the "social" are locked in an explanatory zero-sum game in which any ground ceded to the former diminishes the value of the later (Freese et al. 2003). But even if sociologists (and by extension demographers) did banish "biological" explanations of social behavior from their own forums, swelling interest in the topic would still exist elsewhere in the academy, as would a strong flourishing of curiosity among the general public (Freese et al. 2003). What separates biological perspectives in sociology (sociobiology) and demography (biodemography) from their more conventional alternatives is not whether biological perspectives on sociological or demographic questions are correct but how useful specifically biologically-minded thinking and experimental methods are for understanding human demography.

In the perennial struggle by all disciplines including demography to define and renew themselves and to ensure their relevance in an ever-changing world, each disciplines is always

faced with decisions regarding whether to move in new directions. As Foster (Foster 2000) notes, demography, like other social sciences, is slowly coming to terms with important truths that the biological sciences have proved beyond any doubt—that both the human mind and human behaviors are as much products of biological evolution as is the human body. Wilson (Wilson 1998) noted that human beings may be unique in their degree of behavioral plasticity and in their possession of language and self-awareness, but all of the known human systems—biological and social—taken together form only a small subset of these displayed by the thousands of living species. We believe that the integration of biology into demography through the emerging field of biological demography will provide a deeper understanding of demographic processes and thus will offer insights into which patterns are common to a broad range of organisms and thus which demographic patterns are uniquely human.

Model System

Inasmuch as demography is concerned with whole-animal phenomena (birth; death), model systems (e.g. nematode worm; fruit flies; laboratory rodents) can be brought to bear on fundamental questions concerning the nature of fertility and mortality. However, a stumbling block in mainstream demography for the serious use of these model systems in studying aging has been the mistaken belief that, because causes of death in humans are unrelated to causes of death in non-human species (particularly in invertebrates such as nematodes and fruit flies), little can be learned from detailed knowledge of age-specific mortality in these model species. This perspective is based on a theory familiar to most demographers—the “theory of the underlying cause” in public health and medicine which states that if the starting point of a train of events leading to death is known (e.g. cancer), death can be averted by preventing the initiating cause from operating (Moriyama 1956). For aging research the problem with this perspective is that

death is seen as a single force—the skeleton with the scythe. A more apt characterization that applies to deaths in all species is given by Kannesto who notes that deaths are better viewed as the outcome of a crowd of “little devils”; individual potential or probabalistic causes of death, sometimes hunting in packs and reinforcing each other’s efforts, at other times independent (Kannisto 1991). Inasmuch as underlying causes of death are frequently context-specific, difficult to distinguish from immediate causes, and their post-mortem identification in humans is often arbitrary (in invertebrates virtually impossible), studying the causes of death often provides little insight into the nature of aging. If aging is considered as a varying pattern of vulnerability to genetic and environmental insults, then the most important use of model species in both teaching and research on the demography of aging is to interpret their age patterns of mortality as proxy indicators of frailty. That is, different model systems can be used to address questions at different levels of demographic generality.

Levels of Specificity

The demographic profiles of humans have characteristics typical of a wide variety of organisms due to similarity in evolutionary selection pressures. For example, the characteristic of higher male than female mortality during prime reproductive ages is typical in sexually reproducing animals of a large number of vertebrate and invertebrate species. The pattern is an evolutionary result of sexual selection on males and, as such, is a *general characteristic* of a large number of species. Other observed general characteristics include the variable rate of change in mortality with age (rates that decline after earliest stage and then increase with age) and a slowing of mortality at the most advanced ages (Vaupel et al. 1998). Given such generalities, there are also characteristics of mortality profiles that pertain more specifically to a

particular species (or other taxonomic group). Such species level characteristics are imposed on some general pattern.

The mortality experience for humans can thus be considered at two levels. The *general level* exhibits a decline after infancy, increases through the reproductive life span (the overall U-shaped trajectory), and a sex differential. The *specific level* pertains to details of the mortality experience unique to humans including the actual probabilities of death by age, inflection points of age-specific mortality, the cause-specific probabilities of death, and the age-specific pattern of the sex differential. The observed mortality pattern is a combination of the evolutionary components of the trajectory (which will be common to a large number of species with overlapping life history characteristics) and the proximate age and sex-specific factors contributing to mortality under certain conditions. For example, under contemporary conditions male reproductive competition selects for riskier behavior and results in deaths due to accidents and homicides during early adulthood. The general and specific components of any population's mortality schedule can only be determined through studies using model systems; that is, the use of experimental demography and comparative biology.

Emerging Areas of Biological-Demographic Research: Selected Examples

Evolutionary demography

How long do individuals in different species live? How fecund are they? How big do they grow. Such questions about the age-trajectories of mortality, fertility and growth are of fundamental interest to biological demographers, as well as to life-history biologists and evolutionary theorists. Although there is a vast empirical literature about these age-trajectories, there are remarkably few species for which reliable life tables are available. Furthermore, much fundamental work needs to be done to develop theory--and demographers can contribute to this

work, as evidenced by contributions by Shripad Tuljapurkar (Tuljapurkar 1990; Tuljapurkar 1997), Kenneth Wachter (Wachter 1999), Ronald Lee (Lee 2003) and James Vaupel and co-workers (Vaupel et al. 2004). Lotka, as discussed earlier, pioneered research in evolutionary demography, but following his seminal contributions in the 1920s and 1930s demographers turned to other topics. The recent resurgence of interest in evolutionary demography (now nicknamed evo-demo) suggests that this area may become one of the most interesting and important branches of all demography. This potential is enhanced by the fundamental importance of demography in evolution, as briefly explained in the following paragraph.

Nothing in biology, Dobzhansky asserted, makes sense except in the light of evolution. An equally valid overstatement is that nothing in evolution can be understood except in the light of demography (Dobzhansky 1973). Evolution is driven by population dynamics governed by age-schedules of fertility and survival. Lotka emphasized this. Since his pathbreaking research, models of the evolution of fertility, mortality and other life-history patterns have been based on stable population theory. Lotka's equation

$$\int_0^{\omega} e^{-ra} l(a) m(a) da = 1 \qquad (1)$$

specifies the intrinsic growth rate, r, of a closed population, typically of females, as a function of the proportion, $l(a)$, of newborns surviving to age a and age-specific maternity (or fertility), $m(a)$. If a new subspecies emerges as a result of mutation, then the subspecies is assumed to have an evolutionary advantage if its intrinsic growth rate is greater than that of other subspecies.

Closely related to evolutionary demography is the field of research at the intersection of demography and life-history theory. Life-history theory in biology is concerned with explaining evolutionary fitness in relationship to species-specific characteristics such as age at maturity, age

at fecundity, clutch or litter size, size at birth and age-specific survival rates across species. Biological demography is thus inextricably linked to life history theory because analysis of a species' life history traits must ultimately be considered relative to their effects on birth and/or death rates. Whereas demographers concerned with human populations usually consider birth and death separately (though with some notable exceptions such as (Montgomery and Cohen 1998)), life history theorists are concerned with the fitness implications of particular sets of age-specific birth and death rates as defined by the intrinsic rate of population increase (as discussed above; also see (Fisher 1958)). The seminal papers on life-history theory in the population biology, ecology and evolution literature includes papers on the population consequences of life history traits (Cole. 1954), the use of the Lotka equation to evaluate insect populations (Birch 1948), and on the sensitivity of changes in different life history traits such as age of first reproduction and total fecundity on the intrinsic rate of increase (Lewontin 1965). Recent papers by Ricklefs (Ricklefs and Scheuerlein 2003), Guillard (Gaillard et al. 2003), and Harshman (Harshman 2003) consider life history traits in the context of life span and aging. Recent papers by Hillard Kaplan and his anthropology colleagues (Kaplan 1997; Kaplan et al. 2003; Kaplan and Lancaster 2003) exemplify how life history theory can be brought to bear on important questions concerned with human demography, embodied capital, and the evolution of our extraordinary life span.

Genetic and genomic demography

Biological-demographic concepts can be brought to bear on questions in genetics and genomics in at least two broad contexts. The first is concerned with human demographic history. The genome of our species preserves a record of population dynamics—changes in size and of subdivisions into partially isolated demes (Harpending 2003). Genetic studies suggest that our

species is derived from a small population of perhaps only several thousands of individual that underwent dramatic demographic expansion during the last interglacial period approximately 100,000 years ago (Harpending 2003; Stringer and Andrews 1988). There are several issues in human demography and genetics for which the genetic evidence of a small founding population and subsequent rapid growth are important including (Reich and Goldstein 1998): (1) genetic evidence provides clear support for the 'Garden of Eden' model of modern human origins for which we are the outcome of a speciation event in a small population; (2) human demographic history is the underlying determinant of the distribution of genetic diversity in our species. Thus diversity should be recent rather than ancient and thus localized rather than dispersed throughout our species; and (3) a history of rapid expansion and colonization of most of the earth suggests that our species has from the beginning been ecologically disruptive. The second context in which biological-demographic concepts can be brought to bear on genetics and genomics is in biomedical and health aspects of contemporary populations (Ewbank 2000). We discuss this research in the section, below, on biomedical demography.

Paleodemography

Anthropology and demography have natural affinities since both fields are concerned primarily with humans and with vital events including birth, death and migration (Spuhler 1959; Weiss 1973). Skeletal remains are the source of information about prehistoric populations regarding sex, age at death, lifetime morbidity and nutrition, as well as, for women, number of children born. Hence, a main focus on paleodemography is determining how to extract more information from bones. This requires a sophisticated understanding of biology as well as facility with methods of using physical indicators to determine sex and estimate age at death and other variables. A promising recent advance has been the development, by Ursula Wittwer-backofen

and Jutta Gampe, of methods to count annual rings deposited in teeth as a way of determining age at death. (Roughly similar methods can be used to estimate the age of animals in the wild, with teeth used for mammals and otoliths, ear bones, for fish). Lesions in bones and minerals in teeth and bones can shed light on health and nutritional histories. Information about human population development for the long period during which written records were scarce or nonexistent thus hinges on biological information.

Ecological biodemography

Four studies concerned with the biodemography of wild populations of organisms underscore the importance of ecological studies. The first of these studies is one on field aging rates of the Virginia opossum, *Didelphis virginiana*, (Austad 1993). The study was designed to test the hypothesis "…that populations historically subjected to low rates of environmentally-imposed mortality will ultimately evolve senescence that is retarded in relation to that of populations historically subjected to higher mortality rates." Because islands have reduced predation relative to the mainland, theory predicts that rates of aging will be lower in the insular population. Consistent with this prediction, Austad (Austad 1993) reported reduced senescence for the island population based on physiological measures of aging.

A second series of studies were conducted by David Reznick from UC Riverside who developed a model system for studying the ecology and evolution of longevity in guppies—a small freshwater fish from the northeastern coast of South America and some neighboring Caribbean islands (Reznick et al. 1997). Reznick manipulated field predation rates on adults, and over evolutionary time observed accelerated maturation rates, increased allocation to reproduction, and changes in the size and interval of litters. Reznick's most generalized finding is that environment shapes life span in guppies—the life span of guppies recovered from streams

that supported predator populations whether naturally or through deliberate introductions, was shorter than those in streams in which predators were not present.

The third biodemographic study was by Marc Tatar and co-workers (Tatar et al. 1997) characterized differences in senescence among populations of grasshoppers that occur along an altitudinal gradient in the Sierra Nevada, California. Experimental males from five populations of the grasshopper *Melanoplus sanguinipes/devastat*or sibling species complex were collected along an altitudinal gradient in the Sierra Nevada, California. Tatar and his associates found differences in the physiological capacity to survive in a sheltered, common environment revealed genetic differences in underlying rates of senescence, providing maternal effects do not affect the rate of aging in offspring.

A fourth study of aging in the wild was by Deborah Roach on the perennial plant, *Plantago lanceolata,* using an initial cohort of 10,000 individuals in a natural field environment (Roach 2003). In order to separate the effects of the environment- and age-dependent factors on mortality, additional cohorts were planted in the field over the next three years for a total of 27,000 plants. The results demonstrated that demographic patterns in natural populations are strongly influenced by seasonal and yearly environmental variation, particularly temperature and rainfall. Her study also demonstrated that there is an interdependence of demographic patterns across life stages. Cohorts established in different years showed different patterns of mortality, and the history of mortality within a cohort was critical to late-age demographic patterns. This study showed that age-dependent patterns of mortality can be masked by age-independent environmental factors and that to study aging in a natural population requires one to account for these other influences on mortality. A covariate regression analysis was thus used to determine the age-dependent risk of mortality for this field population (Roach and Gampe, submitted).

Several factors including microsite spatial location, temperature, rainfall, reproduction, size, and genetics were all found to significantly influence mortality in the field. When all of these factors were accounted for in the regression model, there was no evidence for an increased risk of dying with age. These results suggest that increasing size after reproductive maturity may allow species to escape from demographic senescence. An additional greenhouse study contrasting field-grown plants with 1,000 plants grown in the greenhouse, has demonstrated the remarkable plasticity of mortality patterns (Roach 2001). Over a period of four years, mortality was 6% in the greenhouse and 91% for similarly aged plants in the field. Given these contrasting patterns of mortality, individuals in natural populations will thus clearly never experience the extreme old ages of individuals studied under controlled environmental conditions.

BIOMEDICAL DEMOGRAPHY

As noted at the outset of this chapter, biodemography pertains to two different fields, which we call biological demography and biomedical demography. These two fields are as distinct as biology is from biomedicine. We have elected in this chapter to emphasize the concepts and findings of biological demography, in part because the concepts and findings are less familiar to most demographers. Let us now, however, turn to the other branch of biodemography.

The number of demographers working in the area of biomedical demography is at least as large as the number working on biological demography. Grant funding is substantially greater and publications are at least as numerous. The field of biomedical demography is innovative and important, with great potential for making contributions that help improve public health. The field can essentially be characterized as the interface between demography and epidemiology. Demography and epidemiology intersect and overlap. Demographers more frequently focus on

how diseases and disabilities influence the structure and dynamics of a population, whereas most epidemiologists are typically concerned with how population patterns of a specific disease of interest can shed light on the etiology, prevention and cure of the disease. In any case, many demographers have acquired substantial knowledge of the biology of various diseases and disabilities and have developed models of morbidity and mortality. Some of these models relate disease and disability patterns and trends in a population to consequences for health-care systems. Demographers and the epidemiologists are collaborating on designing better surveys, questionnaires, and health measurements.

The field of biomedical demography emerged over the past two decades and is now flourishing. This development was greatly fostered by funding from the Behavioral and Social Science branch of the U.S. National Institute on Aging. The head of this branch, Richard Suzman, deserves great credit for recognizing and supporting the role of demographers in biomedical research. Other sources of inspiration and funding have been the Italian National Institute on Aging, headed by Claudio Franceschi, and the epidemiology and demography program at the University of Southern Denmark, currently under the leadership of Kaare Christensen and Bernard Jeune.

A key event in the history of biomedical demography was a National Research Council workshop in 2000 and called "*Cells and Surveys: Should Biological Measures be Included in Social Science Research*?" The workshop was organized and chaired by Caleb Finch, James Vaupel and Kevin Kinsella; they also edited the resulting volume (Finch et al. 2000). The workshop sought to address questions such as: What can social science in general and demography in particular reasonably expect to learn from biomedical information? Which genetic, pedigree, historical, and environmental data ought to be collected in order to be most

useful to a wide range of scientists? The edited volume that was published from this workshop (Finch et al. 2000) included chapters concerned with the use of bioindicators in demographic and social research, the potential of using genetic information in demography, research on aging human subjects, the relevance of animal models for human populations, value-added survey research and consent and privacy issues.

Currently several major research projects are underway that are headed or co-headed by biomedical demographers. In the United States the three most notable are the Health and Retirement Survey (HRS), the National Long Term Care Survey (NLTCS), and the MacArthur Study of Successful Aging; Beth Soldo played a major role in designing the HRS, Kenneth Manton has long directed the NLTCS, and Eileen Crimmins, Mark Haywood and Burt Singer have worked with the MacArthur data. The very large Chinese Longitudinal Survey of Healthy Longevity was devised by Zeng Yi and James Vaupel. Vaupel (with colleagues such as Anatoli Yashin) also participated in the design, funding and analysis of large longitudinal studies of aging among older Danish twins, very old Sardinians, and elderly Russians living in Moscow and St. Petersburg. Maxine Weinstein and Noreen Goldman have been leaders of the Taiwan Study of the Elderly (Weinstein and Willis 2000).

One of the main contributions of biomedical demographers has been the development of powerful models. Kenneth Manton has played a leadership role in the elaboration of dynamic models for analyzing complicated longitudinal data; he has been assisted by colleagues such as Max Woodbury, Eric Stallard and Anatoli Yashin. The publications of Manton and colleagues are very numerous; one helpful overview is Manton and Yashin (Manton and Yashin 2000). Also notable are the modeling contributions of Douglas Ewbank (Ewbank 2000). (In this regard, let us

parenthetically note that biological demographers, e.g., (Carey et al. 1998) and (Müller et al. 1997) have also contributed some useful new statistical methods).

Demographers over the past half century have increasingly become involved with the design of surveys and the analysis of survey data, especially pertaining to fertility or morbidity and mortality. Recently various kinds of physical measurements (such as height and weight), physiological measurements (of blood pressure, cholesterol levels, etc.), nutritional status (assessed by analysis of blood or urine and other methods), physical performance (e.g., hand-grip strength or ability to pick a coin up from the floor), and genetic makeup (as determined by analysis of DNA) have been added to surveys, including those conducted by Kaare Christensen, Noreen Goldman, Maxine Weinstein, Zeng Yi and others. Such biological measurements can be used as covariates in demographic analyses in much the same way that social and economic information is used: developing such analysis is an important activity of biomedical demographers (Finch et al. 2000).

In particular, there has been rapid growth of interest in using genetic information in medical-demographic research (Ewbank 2000). Particularly exciting is the use information from DNA about specific genes, as in research by Ewbank (2001), Vaupel (Gerdes et al. 2000), and Yashin (Yashin et al. 2000). Information from DNA about genetic polymorphisms (i.e., mutations) can be used to determine the genetic structure of a population and to make inferences about the influence of migration and inbreeding on the population. A central goal of such "molecular demography" is to identify genetic polymorphisms that affect mortality, morbidity, functioning, fecundity, and other sources of demographic change. Much of this research to date, as illustrated by the articles by Ewbank, Vaupel and Yashin cited above, has focused on finding genetic variants that influence longevity. This relationship can be studied by analyzing changes

with age in the proportion of survivors who have some specific allele (i.e., version of a gene). If in a given cohort the allele becomes more frequent with age, that allele may be associated with lower mortality.

It should not be forgotten, however, that much can be learned about genetics even if DNA is unavailable. The genetic and common environment components of these variations--in life spans, fertility, and other demographic characteristics--can be analyzed in humans using demographic data on twins, siblings, cousins, and other relatives of various degree. These data are available in genealogies and in twin, household, parish, and other populations registries. What is necessary is to have information about the proportion of genes shared by two individuals and about shared nongenetic influences. Analysis of variance methods, correlated frailty approaches, and nested event-history models have been applied by demographers. Hans-Peter Kohler (Kohler and Rodgers 2003) has studied how much of the variation in number of children can be attributed to genetic variation in family size preferences among potential parents, and Anatoli Yashin has analyzed genetic variation as it related to susceptibility to various diseases and to mortality in general (Yashin and Iachine 1997; Yashin et al. 2001).

In sum, both the biomedical-demography branch of biodemography and the biological-demography branch are vibrant areas of demographic research that are rapidly growing and that have great potential to enrich and enlarge the domain of demography. Not only can demographers can learn much from biologists and epidemiologists, but demographers can contribute much to research on life in general (as opposed to humans in particular) and to research on population health.

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Table 1. The emerging research agenda for biodemography with cross-cutting themes from both biological demography and biomedical demography.

Level/Sub-levels	Concept/Example(s)
Level I: Molecular to Physiological Biodemography	
	Level I is concerned with processes at the lower levels of biological organization from the molecular to the physiological (Finch et al. 2000); includes basic research on aging and longevity with model organisms as well as the results of studies such as clinical assays involving determination of handgrip and lung capacity and body fluids such as urine and blood; demographic approach to health analysis includes some indicators of 'biology' which are biological risk factors (Crimmins and Seeman 2000);
Molecular	Advances in technology will likely make it possible to carry out molecular screening of a large number of molecules in body fluids or tissue samples that may identify genetic variation or be markers of disease processes (Burns et al. 1998; Halter and Reuben 2000); molecular techniques provide tools for investigating questions about the evolution of humans including phylogenetic relationships among subpopulations; demographic implications of medically assisted reproduction and pre-implantation diagnostics (McClure 1996); medical implications of human genome project(Collins 1999) and demographic outcome
Genetic	Use of twins or other related individuals to control for unobserved heterogeneity associated with genetics; analyses of data on the genetics of individuals or gene frequencies for populations including exploration of genes that may explain geographic differences in individual response to medications (Wallace 1997); demographic implications of pre-implantation and fetal diagnosis (Holzgreve and Hahn 2003); determination of the risk of specific diseases in individuals; research on the genetic basis for common diseases and mortality will benefit from application of multistate modeling Also research on the determinants of health and behaviors could expand to include controls for genetic differences (Ewbank 2000); genetic determinants of longevity in model organisms including nematodes (Johnson 1990; Kenyon 1997) and *Drosophila* (Curtsinger et al. 1992; Harshman 2003; Helfand and Inouye 2002),

Table 1 (continued).

Level/Sub-levels	Concept/Example(s)
Genomic	Include research on origins of human populations and ancient migration streams, the role of evolution in human history, differences in migration patterns of males and females, historical demography of cultures with ancient roots (Cavalli-Sforza et al. 1994; Owens and King 1999). Genome-level basis for disease patterns in human populations; study of population-level genomics—the interface between population genetics, molecular biology and demography (Black et al. 2001; Harpending 2003; Harpending and Rogers 2000)
Cellular	Assays can be used on cells to indicate their health and level of functioning (Halter and Reuben 2000). For example, specific cells can be isolated from blood or tissue samples for testing functional capability such as white blood cells responsible for initiating inflammation, red blood cells for their ability to produce clotting proteins and skin, muscle and fat cells to shed light on their functional characteristics.
Organ	Clinical measurements of body fluids provide important information on the functioning of many organs. For example, blood levels of thyroid hormones provides measures of over- or under-function of the thyroid gland (Halter and Reuben 2000); noninvasive technology documents cardiac arrhythmias and fluctuations in blood pressure; sleep monitoring equipment can be used to document nocturnal activity and sleep patterns; simple mechanical devices are available to estimate pulmonary (lung) function
Physiological	Longevity response of animals to caloric restriction requires an understanding of how animals modulate their metabolic rates when subjected to food shortages (Feder et al. 2000); physiology-to-gene approaches where goal is to find the genetic basis for physiological response underlying longevity; gene-to-physiology approach where goal is to examine the performance and fitness implication of discrete genes or products they encode (e.g. alcohol dehydrogenase on ethanol tolerance); understanding of allostatic load which is the cost of chronic exposure to fluctuating or heightened neural or neuroendocrine response resulting from repeated or chronic environmental challenge that an individual reacts to as being particularly stressful (McEwen and Stellar 1993); late-life influence of pre-natal environment (Barker 1994)

Table 1 (continued).

Level/Sub-levels	Concept/Example(s)
Level II: Individual-, Cohort- and Kinship-level Biodemography	
	Level II is concerned with processes involving biological organization of whole-organism and three levels or types of groupings—the cohort which is group experiencing same event (e.g. birth; marriage), the family which consists of nuclear, stem and extended family and thus grades into more extensive kinship relations including ablineal and colineal kin.
Individual	Integration of different kinds of ages including biological (e.g. functional capabilities), social (i.e. roles and habits relative to others) and psychological (e.g. adaptive capacities such as memory, learning and emotions) age in life course analysis (Settersten and Mayer 1997); whereas life course currently refers to the "social processes extending over the individual life span…" (Settersten and Mayer 1997), a biodemographic agenda will incorporate an understanding of biological processes as well since the biological (reproduction) and social (marriage; family creation) are inextricably intertwined; rescaling the life cycle as life expectancy increases (Lee and Goldstein 2003).
Birth & reproduction	Encompasses interconnections of the biology of reproduction and the demography of individuals and family formation (Bulatao and Casterine 2001; Wachter and Bulato 2003). Includes genetic influences on fertility (Kohler and Rodgers 2003; Rutter 2003), basic questions regarding pair-bonding in monogamous species (Young 2003), mediation of physiological and behavioral processes (Cameron 2003), fertility patterns and behavioral controls in nonhuman primates (Altmann and Alberts 2003), evolution of primate reproductive rates (Ross and Jones 1999); evolutionary perspectives on human fertility and mating patterns (Campbell 2003; Gangestad 2003; Kaplan et al. 2003; Lam 2003; Worthman 2003), and general syntheses of human fertility and reproduction (Bachrach 2001; Hobcraft 2003; Watcher 2003); biological basis for regional and global fertility declines (Bongaarts 2001; Caldwell 2001)

Table 1 (continued).

Level/Sub-levels	Concept/Example(s)
Mortality & longevity	Trajectories of mortality at post-reproductive and advanced ages (Vaupel 1997; Vaupel 2003; Vaupel et al. 1998); models examining relationship between mortality cause-elimination and human life expectancy (Olshansky et al. 1990); reliability theories of aging and longevity (Gavrilov and Gavrilova 2001); the elderly in nature (Austad 1997; Carey and Gruenfelder 1997; Kaplan 1997; Lee 1997), evolutionary theory and senescence (Johnson and Shook 1997; Partridge 1997; Rose 1997; Tuljapurkar 1997); interspecies differences in life span distribution (Horiuchi 2003); comparative life table analysis (Deevey 1947), primate life tables (Gage 1998), and comparative demography of life spans (Carey and Judge 2000);
Birth-Death Interactions	Re-visitation of cost of reproduction concepts (Bell and Koufopanou 1986; Carey 2003b; Reznick 1985); fundamental relationship between early reproduction and late-life mortality (Müller et al. 2001; Müller et al. 2002); effect of child's death on birth spacing, fertility, and fertility transition (Montgomery and Cohen 1998)
Morbidity/frailty	Medical demography—the study of chronic disease, disability, and mortality in mature and aging populations including interaction of disability dynamics and mortality (Manton and Stallard 1994); evolutionary (Darwinian) medicine—approaches to human health based on knowledge of human evolutionary history (Trevathan et al. 1999; Williams and Nesse 1991); natural history of disease stages and the life cycle; comorbidity; cause-elimination models (Palloni 2001); general need to develop sets of proximate biological factors related to health outcomes based on knowledge of biology and the relationship between bioindicators, demographic variables and health outcomes (Crimmins et al. 1996; Lollar and Crews 2003); use of studies on both captive and free-ranging animals populations for investigating the maintenance of allostasis, the cascade of events leading to allostatic load (McEwen and Stellar 1993), and biopsychosocial, pre-disease pathways to diverse health outcomes (Singer and Ryff 2001); morbidity and aging in non-human species including primate gerontology (DeRousseau 1994) and insect frailty studies (Papadopoulos et al. 2002)

Table 1 (continued).

Level/Sub-levels	Concept/Example(s)
Migration/movement	Integration of conceptual and empirical framework developed in ecology for dispersal (movement affecting spatial pattern) and migration (mass directional movement) to demography including biological and behavioral basis for age-specific patterns of migration and dispersal {Cade, 2003 #195; Rogers, 1984 #156; Rogers, 1985 #157; Begon, 1996 #158
Family and Kin	Desired family size and the course of fertility (Bacci 2001; Vogler 2000); patterns of availability and access of elderly to kin (Wolf 1994); two-sex demography (Pollak 1986); biodemography of parental care (Clutton-Brock 1991) and parental behavior (Numan 1998); family and population implications of reprogenetics—modification of germ-line DNA (Kollek 2003); comparative socioecology of kinship bonding and mating systems (Foley 1999)
Level III: Population, Ecological and Evolutionary Biodemography	
	Level III is concerned with levels of organization and processes above the individual including populations (groups of individuals coexisting at a given moment), ecological (interrelationship of organisms and their surroundings), and evolutionary (the descent, with modifications, of different lineages from common ancestors). Biodemography is inextricably linked to all of these organizational groupings since vital rates and population processes underlie the dynamics of change at all levels.
Population principles	Theory of population dynamics (Preston et al. 2001) and applications to both humans (Keyfitz 1977; Shryock and Siegel 1976) and non-human species (Caswell 1989); theoretical basis for evolution of life span and aging (Orzack 2003); demography of growth rate (Mangel 2003);
Human populations	Sociobiological and anthropological perspectives on health (Nguyen and Peschard 2003); evolution of human life span (Kaplan et al. 2003; Kaplan and Lancaster 2003); anthropological demography (Hill and Kaplan 1999) including questions regarding birth and death rates of indigenous peoples, population sex ratios in primitive societies, ages at onset, termination of reproduction and cultural comparisons between foragers versus pastorals (Ellison 2001; Hill and Hurtado 1996); extraordinary longevity in human populations (Robine 2003; Robine and Saito 2003; Wilmoth and Robine 2003); limits to world population (Cohen 1995);

Table 1 (continued).

Level/Sub-levels	Concept/Example(s)
Non-human populations	Life history theory in biodemographic contexts (Caswell 1989; Cole. 1954; Tuljapurkar 1990); studies of geographic structure involving both demography and genetics to examine the distribution of genotypes within and between populations (Roderick 1996; Slatkin 1987); use of social insects as models and concepts of sociobiology (Wilson 1971; Wilson 1975) to gain fundamental insights into social aspects of aging, longevity, fertility, and intra- and intergenerational transfer (Lee 2003; Rueppell et al. 2004); ecological correlates of life span and hazard rates (Gaillard et al. 2003; Ricklefs and Scheuerlein 2003; Wachter 2003); senescence and mortality in field and laboratory populations of plants (Roach 2001; Roach 2003)
Ecological biodemography	Conservation biodemography (Young and Clarke 2000b) and biodemography of invasive species (Sakai et al. 2001) including minimum viable populations (Soule 1987), demography of harvesting (Carey 1993; Getz and Haight 1989); metapopulation analysis (Hastings and Harrison 1994; Thrall et al. 2000), demographic toxicology (Stark and Banks 2003), demographic effects of habitat fragmentation (Young and Clarke 2000a)
Evolutionary biodemography	Understanding the processes of evolution informs every area of biology including biodemography; concerned with the interface of demography, genetics and evolution in age-structured populations (Charlesworth 1994); evolution of life history traits and trade-offs between birth and death (Stearns 1992); accounting for the evolution of short or long life span (Carey 2003a); post-Darwinian longevity (Vaupel 2003); understanding the underlying demography related to the unbroken chains of descent of all organisms from viruses to redwoods to humans (Meagher and Futuyma 2001);