Working Paper

MORTALITY AND AGING IN A HETEROGENEOUS POPULATION: A STOCHASTIC PROCESS MODEL WITH OBSERVED AND UNOBSERVED VARIABLES

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FOREWORD

Low fertility levels in IIASA countries are creating aging populations whose demands for health care and income maintenance (social security) will increase to unprecedented levels, thereby calling forth policies that will seek to promote increased family care and worklife flexibility. The new Population Program will examine current patterns of population aging and changing lifestyles in IIASA countries, project the needs for health and income support that such patterns are likely to generate during the next several decades, and consider alternative family and employment policies that might reduce the social costs of meeting these needs.

A central feature of the Population Program's research agenda is the development of a theoretical model of human aging and mortality. This paper reports the results of some preliminary efforts along that line. In it, a Soviet mathematician, Dr. Yashin, collaborating with a demographer and a policy analyst from the United States, describes a multidimensional stochastic process model that generalizes earlier models of aging dynamics. The authors introduce the effects of non-Markovian behavior, unobservable variables, and measurement error, showing how additional information about state variables influences an observer's understanding of temporal changes in the physiological system.

Andrei Rogers
Leader
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ABSTRACT

A number of multivariate stochastic process models have been developed to represent human physiological aging and mortality. In this paper, we extend those efforts by considering the effects of unobserved state variables on the age trajectory of physiological parameters. This is accomplished by deriving the Kolmogorov-Fokker-Planck equations for the distribution of the state variables conditionally on the process of the observed state variables. Proofs are given that this form of the process will preserve the Gaussian properties of the distribution. Strategies for estimating the parameters of the distribution of the unobserved variable are suggested based on an extension of the theory of Kalman filters to include systematic mortality selection. Implications of individual differences on the trajectories of the unobserved process for observed aging changes are discussed as well as the consequences of such modeling for dealing with other types of processes in heterogeneous populations.

CONTENTS

I. INTRODUCTION

A. Background

There have been a number of efforts to develop a theoretical model for human aging and mortality. The law of mortality due to Gompertz (1825) was an early such attempt. Here, human mortality is modeled as a uni-dimensional failure process based on a constant loss of vitality. It is interesting that the "Gompertzian model" of human aging dynamics continues to be applied especially for mortality at advanced ages (Fries, 1980).

Such simple "failure process" models of human aging and mortality, although perhaps useful descriptive tools, are not totally satisfactory models of human aging processes for a number of reasons. First, they imply that human aging processes are uni-dimensional. It seems extremely unlikely that the physiological dynamics of the genetic and environmental determinants of human aging could be described by a uni-dimensional process. Second, considerable empirical evidence has accumulated to show that human mortality patterns at later ages are not well-described by the Gompertz function (e.g., Horiuchi and Coale,1983; Wilkin, 1982). Third, we often have a wide range of physiological covariates available for analysis from longitudinally followed populations. The simple model of Gompertzian aging dynamics cannot use information on those covariates. Indeed, such models do not explicitly describe the physiological mechanisms underlying the aging process. Thus, it is necessary to develop models which can successfully utilize this information.

A number of models of human aging and mortality have been developed which do describe the physiological mechanisms underlying aging changes. Several of these are reported in Chapter 7 of Strehler (1977). Perhaps one of the most successful of these models was due to Sacher and Trucco

(1962). This model describes physiological aging as a process by which homeostasis was maintained in a multi-variate state space. Mortality was described in the model in one of two ways. First, if one assumed that the state space was of high dimensionality, mortality was described as a permanent loss of homeostasis due to the exceedance of some physiological threshold. Since such a formulation would only be of theoretical use, it was argued that mortality might also be modeled as an absorbing boundary.

Such absorbing boundary formulations of mortality lead to serious difficulty in empirical applications since: a.) they imply that one must deal with truncated distribution functions, and b.) they represent mortality as a deterministic function of the state space variables. To deal with this problem, Woodbury and Manton (1977) presented a theory of human aging and mortality composed of two parallel processes. The first is a multivariate stochastic process describing the change in the distribution function for the state variables. The second is a jump process which represents mortality as a probabilistic function of an individual's state space values. This model has been successfully applied to both epidemiological studies of chronic disease risk (Woodbury et al., 1979) and to longitudinal studies of normal aging processes (Woodbury and Manton, 1983; Manton and Woodbury, 1983).

In the Woodbury and Manton (1977) model, it is assumed that all relevant state variables are observed. Clearly, in practice such an assumption is only an approximation. Consequently, in this paper we extend the Woodbury and Manton theory of human aging and mortality to include explicit consideration of the effects of unobserved state variables in the process.

B. A Generalization of Aging Dynamics To Deal With Observed and Unobserved State Variables: The Problem

In Woodbury and Manton, a theory of human aging is based on a mathematical model of the change over time of a multivariate distribution function that describes the location of a population in a multidimensional space of state variables. Alternatively, the distribution function can be interpreted as describing the probability that an individual has some set of characteristics at some age. The state space does not include all factors relevant to the time path and survival of an individual. The omitted factors manifest themselves in two ways. First, the movement of an individual in the space is to some extent random: an individual's time path is governed by a set of stochastic (rather than deterministic) differential equations. Second, an individual's position in the space does not determine mortality, but merely the hazard or force of mortality.

Woodbury and Manton describe the change in the multivariate distribution of the state variables by a Kolmogorov-Fokker-Planck (KFP) equation. In the KFP equation, they specify four types of physiological dynamics: drift (i.e., systematic change in mean values), regression (i.e., convergence to mean values, due perhaps to homeostatic tendencies), diffusion (i.e., divergence due to random influences), and mortality selection (i.e., loss from the population of frail individuals). To apply the KFP equation they assume that the process is Markovian. Some aspects of an aging process, however, may depend on an individual's entire life history.

In this paper, we generalize Woodbury and Manton's model to deal with non-Markovian processes, unobservable variables, and measurement error. We present our results in a way designed to show how additional information about the state variables influences an observer's understanding of the temporal change of the physiological system.

Our model assumes that each individual is characterized by a set of variables that change over time. Some of these variables are measured; the rest are not observed over time, but as in the Woodbury-Manton model, some information is available about them. Specifically, we assume knowledge of the probability distribution of the unobserved variables at the initial time zero as well as of the stochastic differential equations describing their random time path. The stochasticity in the aging process is generated by a Wiener (i.e., Brownian motion) process, as well as by the randomness in the initial values of unobserved variables. The force of mortality is a function of an individual's position in the state space.

We deal with the observed variables by developing a form of the KFP equation that describes the change in the distribution of the unobserved variables conditional both on survival to age t <u>and</u> on the trajectories of the observed variables. We then show that if the force of mortality for an individual is a quadratic function of the unobserved variables, it is possible to estimate the means and variances of the unobserved variables over time. The equations used are similar to the Kalman filter equations developed by communication theorists to estimate signals. The equations, however, generalize the usual Kalman filter equations to include mortality.

The force of mortality as a function of age and observed life history can be directly estimated. As noted above, however, estimates based directly on the observed data pertain only to the surviving population and not to the population as a whole or to any homogeneous subgroup within it. The surviving population differs from the entire population because of systematic mortality selection. Specifically, individuals at high mortality risk on the unobserved variables will die off more rapidly and thus will be underrepresented in the surviving population. Thus, to retrieve the parameters of the process for the whole population, or for select individuals, one's model of the process must adjust for selection on both observed and unobserved state variables. We show that, given the estimates of the means and variances of the unobserved variables, one can calculate the force of mortality for individuals at age t with identical observed as well as unobserved characteristics. Thus, the impact on aging and mortality of each of the observed and unobserved variables can be identified.

C. Orientation

Our presentation is organized as follows:

--We describe three different formulations of a model of aging and mortality based on Woodbury and Manton's suggestions. The first formulation describes the process for a single unobserved variable using a simple version of the Woodbury-Manton model. The second formulation shows how the basic process is modified to include observations of time of death. The third formulation introduces a second state variable which is continuously monitored over time. For these three cases, we derive the equations, based on the KFP equation, that give the (conditional) density of the unobserved variable. We discuss how the various increments in information affect the description of the dynamics of the aging and mortality process. In a fourth section of this part of the paper, we sketch two extensions of the model: we allow the stochastic differential equations that describe the trajectories of the variable to depend on the entire history of the observed variable, and we indicate how the model can be generalized to an arbitrary number of observed and unobserved variables.

--We then briefly review the restrictions and assumptions suggested by Woodbury and Manton to estimate the distribution of the unobserved variables. We make some analogous restrictions and assumptions and prove some results concerning the Gaussian form of the distribution. By extending the theory of Kalman filters, we present equations for the mean and variance of this distribution. In addition, we give the equation for calculating the force of mortality of individuals at time t with any specified set of observed and unobserved characteristics.

--Next we discuss applications of the model to empirical studies of aging and mortality processes with observed and unobserved variables.

--We conclude with a discussion of how our model of human aging and mortality relates to other attempts to study the general problem of determining the effects on a stochastic process of systematic population loss due to selection or transition to an alternate state.

II. ALTERNATIVE FORMULATIONS OF A MODEL OF AGING AND MORTALITY

A. The Basic Model

In this section we describe a model of aging and mortality of the general type suggested by Woodbury and Manton (1977). For ease of comparison with the alternative formulations presented below, we describe this model in terms of a single physiological or environmental variable $Y(t)$: generalization to an arbitrary number of variables is straightforward. In addition to the process describing changes in physiological states we will represent time of death by a nonnegative random variable T whose distribution depends on the value of $Y(t)$. Hence, in addition to the evolution of $Y(t)$ described by a stochastic differential equation, the model includes an additional random process that is described by a mortality indicator $I(t)$. The time path of each individual is thus described by $I(t)$ where

$$I(t) = 1 \text{ if } T>t, \text{ otherwise } I(t) = 0, \tag{1}$$

and by $Y(t)$ satisfying

$$dY(t) = a(t,Y(t))\, I(t)dt + b(t,Y(t))\, I(t)\, dW(t). \tag{2}$$

In (2), W is a Wiener process that is independent of the initial value $Y(0)$, which is a random variable with known distribution. It is assumed that the coefficients a and b are known, but that no observations are available on $Y(t)$ or $I(t)$. Note that when an individual dies, the effect of $I(t)$ in (2) is to make further change in the coefficients a and b irrelevant: this is reasonable for physiological processes. In the case of environmental variables, $I(t)$ can be omitted from (2): air temperature does not depend on the survival of a given individual. The conditional distribution of T is given by

$$P(T>t|Y_0^t) = e^{-\int_0^t \mu(s,Y(s))ds}, \tag{3}$$

where μ is a bounded function, assumed known, that can be interpreted as the force of mortality for individuals at time t with characteristic $Y(t)$, and where Y_0^t represents the entire history of Y from time 0 to time t.

The density function of $Y(t)$ may be written as

$$f_t(y) = \frac{\partial}{\partial y} P(Y(t)\leq y,\ T>t) = \frac{\partial}{\partial y} P(Y(t)\leq y,\ I(t)=1). \tag{4}$$

As Woodbury and Manton note, the change in this density function over time is governed by the Kolmogorov-Fokker-Planck equation:

$$\frac{\partial\ f_t(y)}{\partial t} = -\frac{\partial}{\partial y}[a(t,y)\ f_t(y)] + \tfrac{1}{2}\frac{\partial^2}{\partial y^2}[b^2(t,y)\ f_t(y)] - \mu(t,y)\ f_t(y). \tag{5}$$

The three additive terms in this equation reflect the different forces affecting the dynamics of change in the distribution of $Y(t)$. The first term describes the effects usually called drift and regression; the second term, the effects of diffusion; and the third term, the effects of mortality selection.

B. The Model When Death Is Observed

Suppose now that individuals' deaths are observed, so that it is known whether T, the time of death for an individual, exceeds t. Define the conditional density of Y(t) by:

$$f_t^*(y) = \frac{\partial}{\partial y} P(Y(t) \leq y \mid T > t). \tag{6}$$

Then it follows from the more general proof outlined in Appendix A that

$$\frac{\partial f_t^*(y)}{\partial t} = -\frac{\partial}{\partial y}[a(t,y)\; f_t^*(y)] + \tfrac{1}{2}\frac{\partial^2}{\partial y^2}[b^2(t,y)\; f_t^*(y)] - \mu(t,y)\; f_t^*(y) + \bar{\mu}(t)\; f_t^*(y)\;, \tag{7}$$

where

$$\bar{\mu}(t) = E[\mu(t,y) \mid T > t]. \tag{8}$$

This generalization of the KFP equation is similar to (5) except for the additional factor given by (8). This factor, which may be interpreted as the observed force of mortality at time t, can be considered a correction term arising from the additional information known about whether an individual is alive.

C. The Model When Death And A Variable Are Observed

Now suppose that there is an additional physiological or environmental variable X(t) that is observed over time. In particular, suppose that in addition to (1) the following two equations describe the time path of an individual:

$$dY(t) = a(t,Y(t),X(t)) \cdot I(t)dt + b(t,Y(t),X(t)) \cdot I(t)dW_1(t) \tag{9}$$

and

$$dX(t) = A(t,Y(t),X(t)) \cdot I(t)dt + B(t,X(t)) \cdot I(t)dW_2(t)\;, \tag{10}$$

where W_1 and W_2 are Wiener processes independent of each other and of the initial values X(0) and Y(0). Define the conditional density of Y(t) by

$$f_t^{**}(y) = \frac{\partial}{\partial y} P(Y(t) \leq y | T>t,\ X_0^t), \tag{6'}$$

where X_0^t represents the entire history of the process X from time 0 to time t. Then as indicated in Appendix A,

$$\frac{\partial f_t(y)}{\partial t} = -\frac{\partial}{\partial y}[a(t,y,X(t))\ f_t^{**}(y)] + \tfrac{1}{2}\frac{\partial^2}{\partial y^2}[b^2(t,y,X(t))\ f_t^{**}(y)]$$
$$-\mu(t,y,X(t))\ f_t^{**}(y) + \bar{\mu}(t,X_0^t)\ f_t^{**}(y) \tag{11}$$
$$+ f_t^{**}(y) \cdot \{\frac{A(t,y,X(t))-\bar{A}(t,X_0^t)}{B^2(t,X(t))} \cdot (dy_t - \bar{A}(t,X_0^t)dt)\},$$

where

$$\bar{A}(t,X_0^t) = E(A(t,Y(t),X(t))|T>t,\ X_0^t). \tag{12}$$

Note the similarity of (11) to (5) and (7). The additional, final term in (11) describes the effect of observing X(t).

D. <u>Further Extensions Of The Model</u>

The processes considered up until now have been Markovian processes: the coefficients in the stochastic differential equations (2), (9), and (10) depend only on the current values of the variables. That is, it is assumed that the current values on the individual's physiological variables are reasonable approximations of the individuals' physiological "state" and, consequently, will describe the future changes of that state except for stochastic innovations. When X(t) is observed, it is possible to generalize the process to depend on the entire history of X_0^t. This implies that the prior physiological characteristics of the individual, and possibly the trajectory of change of those physiological characteristics, must be included in the definition of physiological state. For example, having elevated blood pressure at the current time may not be sufficient to describe the state of the individual with respect to mortality risks. Risk may be more dependent upon accumulated damage (perhaps represented by the elevation of pressure over a long period of time) or upon extreme values (e.g., the number of times a blood pressure threshold was exceeded). Such processes may be modeled by replacing $X(t)$ in (9), (10), (11) and (12) by X_0^t. A sketch of the proof is given in Appendix A.

Each of the three formulations presented above can be readily extended to the general case of any number of state variables. This extension requires the substitution of the appropriate matrices.

III. ESTIMATING THE UNOBSERVED VARIABLE

Woodbury and Manton (1977) suggest some assumptions and restrictions for estimating the parameters of the observed process. Some of these will be useful for estimating characteristics of the unobserved variables. In the following we apply their general time series approach to the various formulations described above..

A. The Basic Model

Consider the first formulation of the model, presented above in section IIA, in which neither death nor the state variable are observed. This case is primarily of theoretical interest although if enough parameter estimates are available from auxiliary data, the equations below will define the evolution of the distribution of the unobserved variables. Assume that the observed variable follows a Gaussian distribution at time 0. Furthermore, restrict the stochastic equation in (2) as follows:

$$dY(t) = a_0(t) + a_1(t)\ Y(t)dt + b(t)dW_1(t). \tag{13}$$

It is obvious that the distribution of $Y(t)$ is Gaussian at any time t. The mean, $m(t)$, and variance, $\gamma(t)$, of this distribution are given by:

$$\frac{dm(t)}{dt} = a_0(t) + a_1(t)\ m(t) \tag{14}$$

and

$$\frac{d\gamma(t)}{dt} = 2a_1(t)\ \gamma(t) + b^2(t). \tag{15}$$

B. The Model When Only Death Is Observed

Now consider the second formulation presented above. Assume that the unobserved variable follows a Gaussian distribution at time 0 and that the force of mortality is a quadratic function of this variable:

$$\mu(t,Y(t)) = \mu_0(t) + Y(t)\ \mu_1(t) + Y^2(t)\ \mu_2(t). \tag{16}$$

Furthermore, restrict the stochastic differential equation in (2) as follows:

$$dY(t) = I(t) \cdot [a_0(t) + a_1(t)\ Y(t)dt + b(t)dW_1(t)]. \tag{17}$$

It follows that the distribution of $Y(t)$ conditional on $I(t) = 1$ or $T>t$ (in other words, among the surviving population) is Gaussian at any time t: proof of this is a special case of the more general proof sketched in Appendix A; a specific proof may be found in Yashin (1983). The mean, $m(t)$, and variance, $\gamma(t)$, of this distribution are given by:

$$\frac{dm(t)}{dt} = a_0(t) + a_1(t)\ m(t) - \gamma(t)\ \mu_1(t) - 2m(t)\ \gamma(t)\ \mu_2(t) \tag{18}$$

and

$$\frac{d\gamma(t)}{dt} = 2a_1(t)\ \gamma(t) - 2\mu_2(t)\ \gamma^2(t) + b^2(t). \tag{19}$$

Note the additional terms in (18) and (19) compared with (14) and (15). The observed force of mortality is given by the following formula:

$$\bar{\mu}(t) = \mu_0(t) + m(t)\ \mu_1(t) + (m^2(t) + \gamma(t))\ \mu_2(t). \tag{20}$$

If restrictions are placed on the μ's in this formula--e.g., so that they are constant or follow certain specified functional forms--then it may be possible to estimate their values given the observed values of $\bar{\mu}$. Another approach is to restrict (16) to:

$$\mu(t,Y(t)) = Y^2(t) \cdot \mu(t). \tag{21}$$

This constraint is analogous to the formulation in Vaupel et al. (1979). Y^2 corresponds to the variable called "frailty". The formula in (20) reduces to

$$\bar{\mu}(t) = (m^2(t) + \gamma(t)) \cdot \mu(t), \tag{22}$$

so that the time path of $\mu(t)$ can be calculated from the observations of $\bar{\mu}(t)$ and the estimates of $m(t)$ and $\gamma(t)$.

C. The Model When Death And X(t) Are Observed

Suppose now that $X(t)$ is observed. Assume that the distribution of the unobserved $Y(0)$ conditional on the observed $X(0)$ is Gaussian and that the force of mortality is a quadratic function of $Y(t)$:

$$\mu(t,Y(t),X_0^t) = \mu_0(t,X_0^t) + Y(t)\ \mu_1(t,X_0^t) + Y^2(t)\ \mu_2(t,X_0^t). \tag{23}$$

In addition, restrict the stochastic differential equations as follows:

$$dY(t) = [a_0(t,X_0^t) + a_1(t,X_0^t)\ Y(t)]dt + b_1(t,X_0^t)dW_1(t) + b_2(t,X_0^t)dW_2(t) \tag{24}$$

and

$$dX(t) = [A_0(t,X_0^t) + A_1(t,X_0^t)\ Y(t)]dt + B(t,X_0^t)dW_2(t)\ . \tag{25}$$

Note that (24) and (25) are more general than (9) and (10). First, the coefficients may depend on the entire history of X_0^t: this represents the extension to the non-Markovian case. Second, the first equation now depends on both Wiener processes (i.e., W_1 and W_2). This is a straightforward generalization that may be useful in estimation.

As outlined in Appendix B, it follows that the distribution of $Y(t)$ conditional on $X(t)$ and $T>t$ is Gaussian. Furthermore, the mean and variance of this conditional distribution are given by:

$$\begin{aligned} dm(t) = {} & [a_0(t,X_0^t) + a_1(t,X_0^t)\ m(t) - \gamma(t)\ \mu_1(t,X_0^t) - \gamma(t)m(t)\ \mu_2(t,X_0^t)]dt \\ & + [\frac{b_2(t,X_0^t)\ B(t,X_0^t) + A_1(t,X_0^t)\ \gamma(t)}{B^2(t,X_0^t)}] \\ & \cdot [dX(t) - (A_0(t,X_0^t) + A_1(t,X_0^t)m(t))dt]. \end{aligned} \tag{26}$$

and

$$\frac{d\gamma(t)}{dt} = 2[a_1(t,X_0^t) - \frac{b_2(t,X_0^t)}{B(t,X_0^t)} A_1(t,X_0^t) - \mu_2(t,X_0^t)\ \gamma(t)]$$
$$\cdot\ \gamma(t) + b_1^2(t,X_0^t) - \frac{A_1^2(t,X_0^t)}{B^2(t,X_0^t)}\ \gamma(t). \tag{27}$$

These two equations are similar to the previous expressions for the mean and variance in (18) and (19) except for the final terms (and terms arising from the inclusion of W_2 in (24)). These final terms can be viewed as corrections introduced because information is available about X_0^t. The terms will look familiar to students of continuous-time Kalman filters. Indeed, one way of interpreting (26) and (27) is that they generalize the usual Kalman filter equations to include the force of mortality.

The observed force of mortality can be related to the observed variables and the distribution of the unobservable variables by

$$\bar{\mu}(t,X_0^t) = \mu_0(t,X_0^t) + m(t)\ \mu_1(t,X_0^t) + (m^2(t) + \gamma(t))\ \mu_2(t,X_0^t). \tag{28}$$

D. Discrete Time Observations

In most empirical studies, the observed variables are not monitored continuously but are observed from time to time. This section describes how the formulas developed above may be applied to the case of discrete time observations. Assume that the unobserved process is governed by the stochastic differential equation

$$dY(t) = (a_0(t,X) + a_1(t,X)\ Y(t))\ dt + b(t,X)dW_t, \tag{29}$$

where the process X is now the sequence of (t_n,X_n), $n>0$. That is, there is a sequence of observation times $t_1, t_2, \ldots, t_n$, and a sequence of measurements $X_1, X_2, \ldots, X_n$. The X_n sequence can be described by the generating procedure:

$$X_n = A(T_n,X)\ Y(T_n) + D(T_n,X)\ \mathcal{E}_n \tag{30}$$

where $A(t,X)$ and $D(t,X)$ (as well as $a_0(t,X)$, $a_1(t,X)$, $b(t,X)$) are known functions of t and the entire history of the process X up to but not including time t and where $\mathcal{E}_n$ is a sequence of Gaussian-distributed random variables with mean 0 and variance 1. From a straightforward manipulation of (30), we see that the time series of the unobserved variables, $Y(T_n)$ can be generated from the observed time series in X and the assumption of the Gaussian diffusion process, with appropriate normalization, for $Y(T_n)$. Likewise, (30) illustrates how the unobserved variables affect the observed process. As before, we assume that the force of mortality may be represented by

$$\mu(t,X,Y(t)) = \mu_0(t,X) + Y(t)\ \mu_1(t,X) + Y^2(t)\ \mu_2(t,X), \tag{31}$$

where the $\mu_1(t,X)$ are nonnegative, measurable functions of t and the entire history of X up to but not including time t.

By generalizing the method of proof used in Yashin (1980) it can be shown that the conditional distribution of Y(t) given I(t) = 1 (i.e., T>t) and X is Gaussian. The mean and variance of this distribution are:

$$\begin{aligned} m(t) &= m(0) + \int_0^t [a_0(s,X) + a_1(s,X)\ m(s) - \gamma(s)\ \mu_1(s,X) \\ &\quad - \gamma(s)m(s)\ \mu_2(s,X)]ds + \sum_{t_n \le t} A(t_n,X)\ \gamma(t_n)\ \ (A^2(t_n,X)\ \gamma(t_n) \\ &\quad + D^2(t_n,X))^{-1} \cdot (X_n - A(t_n,X)m(t_n)\,. \end{aligned} \tag{32}$$

and

$$\begin{aligned} \gamma(t) &= \gamma(0) + \int_0^t [2a_1(s,X)\ \gamma(s) + b^2(s,X) - 2\mu_2(s,X)\ \gamma^2(s))ds \\ &\quad + \sum_{t_n \le t} \gamma^2(t_n-)\ A^2(t_n,X)\ \ [A^2(t_n,X)\ \gamma(t_n)\ \ + D^2(t_n,X)]^{-1}. \end{aligned} \tag{33}$$

These equations may be viewed as generalizations of both continuous time and discrete time Kalman filter algorithms.

IV. APPLICATIONS

A. <u>General Observations</u>

To use the model empirically, it is necessary to produce estimates of the values of the coefficients in the stochastic differential equations (25) and either (24) or (29). Although discussion of the details of statistical estimation is beyond the scope of this paper, we note that if observations are available on a population of individuals across time and over age, then the coefficients of these equations are estimable given the appropriate identifying constraints. For example, by specifying that in equation (29) certain coefficients can vary by age, but not time (i.e., the constraint of no cohort effects operating through X), we can estimate certain coefficients for (24) if cohort effects do emerge. Alternately, previous theoretical and empirical research may suggest values or functional forms for the coefficients that will facilitate estimation. In particular, there have been a number of longitudinal studies of aging processes (e.g., the first and second Duke Longitudinal studies of normative aging) which can provide estimates of the age rate of decline of a broad range of physiological parameters. These estimates could be employed directly in the equations.

Given the coefficients, (26) and (27) or (32) and (33) permit estimation of the mean and variance of the conditional distribution of the unobserved variable. Equation (28) can then be used as the basis for estimating the force of mortality for an individual with any specified characteristics and at any age. As noted earlier, this estimation might require specifying certain functional forms for μ_0, μ_1, and μ_2. Alternatively, it might be assumed that μ_0 and μ_1 are equal to zero, in which case the values of μ_2 over time can be immediately calculated from the observations of $\bar{\mu}$ over time.

B. Unobserved Risk Factors

The model may be useful in a variety of applications where data are available over time concerning some variables, but there is reason to believe that other significant variables are unobserved. In some cases enough theoretical or empirical knowledge may be available about these unobserved variables so that the initial probability distributions and stochastic differential equations can be specified with some confidence. In such cases estimation of the evolution of the unobserved variables may be of considerable interest. In other cases, it may be suspected that some unmeasured factor such as "frailty" is an important source of heterogeneity in the population. Such a variable may have to be introduced by imposing constraints in the model. For instance, Vaupel et al. (1979) assume that an individual's frailty is constant over age and that the distribution of frailty among individuals follows some simple distributional form. In some studies the unobserved variable may not be of much interest: it may be viewed as a nuisance important only because it obscures the actual relationships among the variables of direct interest.

As a specific example of this kind of application, consider a longitudinal analysis of chronic illness based on the kind of information collected, say, in the Framingham study. Manton et al. (1979) and Woodbury et al. (1979, 1981) present analyses of this sort, based on the insights of the Woodbury-Manton model. In their analyses, the change in coronary heart disease risk factors in the study population was modeled as an autoregressive process adjusted for the effects of systematic mortality selection. It seems likely the population was subject to risk factors not fully represented by the available measurements, i.e., systolic and diastolic blood pressure, serum cholesterol, uric acid, etc. The stochastic differential equations presented here, and the Kalman filter equations generalized to represent the effects of mortality selection offer a range of strategies for a.) estimating the impact of unobserved risk factors, and b.) identifying the "true" effects of observed risk variables.

C. Partially Overlapping Studies

Sometimes longitudinal data are available from several related studies such that some variables are observed in all studies, but other variables are observed in only some studies. Having a set of such studies can greatly facilitate the estimation of the model parameters. For instance, the Woodbury-Manton model has served as the basis for analyses of coronary heart disease risks not only in the Framingham study population, but also in the populations observed in the Duke Longitudinal Study of Aging (Manton and Woodbury, 1983), and of a Kaunas, Lithuania study. Partially overlapping sets of observed variables were available for these three analyses. The Duke study differed from the Framingham study in that uric acid concentrations were not observed, but scores were taken on the Wechsler Adult Intelligence Scale. In the Kaunas study, intelligence test data were not available, but unlike the other data sets, observations were available of smoking behavior and of an index of body mass.

To compare and synthesize such imperfectly coordinated data sets, it may be useful to employ a model that includes all of the variables observed in any of the studies. The model could then be applied to the different studies by specifying which variables were observed and which were not observed. The effects of all of the variables across all of the studies could then be compared. Furthermore, process parameters estimated for an "observable" in one study could be applied to another study where that variable was "unobserved".

D. Measurement Errors and Indirect Measurements

Most variables can only be measured with some error: sometimes the noise can be severe. In other cases, a variable of prime interest can not be observed directly, but a correlated variable can be monitored and used as an index. For instance, the elasticity of blood vessels may be important in coronary heart disease processes, but observations may only be available on blood pressure. Indeed, most of the measurements available in studies of aging processes may only indirectly reflect the underlying physiological state variables.

As noted above, the formulas presented for estimating the mean and variance of the unobserved variables can be interpreted as extensions of the Kalman filter equations developed to detect signals in noisy measurements. Thus, the Kalman filter type equation presented here can be useful in identifying tha true variables of the process, in the face of measurement error or indirect assessment, from studies with multiple measurements taken over time.

E. Assumptions

Efforts to apply the model will, of course, be dependent on the reasonableness of model assumptions for a specific application. In this section, we discuss assumptions and some strategies for extending their applicability to certain situations.

1. Gaussian Distribution

The distribution of the unobserved variables conditional on the observed variables at time zero is assumed to be Gaussian. Furthermore, the model implies that this conditional distribution among survivors will be Gaussian at any time t. For some variables this may not be true, but a transform of a variable may be more or less Gaussian distributed. For example, Manton and Woodbury (1983) use as their variables the logarithms of pulse pressure, diastolic blood pressure, and serum cholesterol level. Consideration of the reasonableness of this assumption must be based on available theoretical insight about the dynamics of the unobserved variable (see Manton and Stallard, 1981).

2. Quadratic Hazard

The force of mortality is assumed to be a quadratic function of the unobserved variables. This assumption is closely tied to the Gaussian assumption, as the following example illustrates. Let $\mu(t,Y)$ be the force of mortality at time t for an individual with unobserved characteristic Y. Suppose

$$\mu(t,Y) = Y^2 \mu(t), \tag{34}$$

where $\mu(t)$ might be interpreted as the force of mortality for some standard individual for whom Y equals one. Now consider an alternative formulation:

$$\mu(t,z) = z\ \mu(t), \tag{35}$$

where z is a characteristic that equals Y^2. This formulation is the one used in the "frailty" model proposed by Vaupel et al. (1979) and applied in studies by Manton et al. (1981) and Horiuchi and Coale (1983). Finally, consider the formulation where

$$\mu(t,x) = \mu(t)\ e^x, \tag{36}$$

where x is a characteristic that equals the logarithm of Y^2. This approach has been adopted in a variety of studies, including Heckman and Singer (1982). Given the appropriate probability distributions, all three formulations can be made equivalent. For instance, the first formulation with Y following a Gaussian distribution with mean zero and variance one is equivalent to the second formulation with z following a Gamma distribution with scale parameter one and shape parameter 0.5.

In some respects the second formulation, involving z, is the most transparent since z can be interpreted as measuring the relative risk of mortality for an individual compared to some "standard" individual. Since Y does not have to be a single variable, but can be a vector of variables, it is possible to consider z defined by

$$z = Y^T \underline{a}\ Y, \tag{37}$$

where $\underline{a}$ is a matrix. In this case, z will have a distribution known as a quadratic form of the Gaussian distribution. Such quadratic forms are very flexible and can take on a variety of shapes. Thus, the assumption that each variable in the unobservable set of variables Y is Gaussian distributed can be readily generalized to the case where the unobserved variables can, in effect, follow a quadratic form of the Gaussian distribution. Biologically the quadratic form of the hazard is reasonable for physiological parameters subject to homeostatic forces. That is, variables that are essential to physiological functioning should have a viable interior range and non-viable external ranges where homeostasis breaks down.

3. Differential Processes

Both the observed and unobserved variables in our model are assumed to be continuous and governed by a differential process. In a variety of studies this may be satisfactory. In some instances, however, categorical variables that are either constant over time or that follow some jumping process may be important. Constant categorical variables, like sex, race, or national origin, can be handled by stratifying the data. Discrete-state variables that jump from one state to another pose a much more difficult problem. Examples of such variables that may be relevant to studies of aging and mortality include marital status, type of employment, place of residence, and such factors as whether an individual is hospitalized or in a nursing home, has had a stroke or a heart attack, has quit smoking, and so on. It is possible to extend the models presented here to the more general case where some of the observed or unobserved variables follow a jumping process as opposed to a differential process.

V. DISCUSSION

In both empirical and theoretical studies of human aging and mortality, the need for modeling individual differences in aging processes has been repeatedly demonstrated (e.g., Strehler, 1977; Economos, 1982; Manton and Woodbury, 1983). Unfortunately, there are many instances where those differences are due to unobserved variables. Indeed, the nature of the sources of these differences, such as differences in the age-related loss of functional "vitality" or the impact on longevity of genetic factors, suggest that difficulties in measurement and conceptualization will dictate that such individual properties will remain at least partially hidden for a long time. Nonetheless, successfully coping with the effects on aging processes of such latent heterogeneity will be a necessary component of adequate models of human aging and mortality. For example, Economos (1982) has argued for the necessity of joining "Simm's idea of statistically distributed individual aging rates" with Gompertz's concept of "accelerated decline of vitality" in order to relate the observed pattern of rates of aging with the observed pattern of the rates of dying. Indeed, the logic by which these concepts are related is that of a diffusion process where temporary sojourns above a threshold value cause the rate of increase in mortality rates to be more rapid than the rate of decline of physiological vitality.

The model we have presented provides a flexible strategy for assessing the impact of such heterogeneity on human aging and mortality processes. In particular, it generalizes the notion of the effects of heterogeneity from that of a fixed distribution to the effects of an unobserved process. Thus, it can lead to an empirical strategy for assessing both function change and mortality which is rich enough to represent the complexity of current conceptual models of human aging and mortality.

We presented our model as a development of the Woodbury-Manton model of aging and mortality published by this journal. Our model can also be viewed as having roots in analyses done by numerous researchers in a variety of disciplines. Often analysts working in the various fields of statistics (e.g., Lundberg, 1940), labor economics (e.g., Blumen, Kogan and McCarthy, 1955), sociology (e.g., Singer and Spilerman, 1974), reliability engineering (e.g., Harris and Singpurwalla, 1968), demography (e.g., Sheps and Menken, 1973), and health policy analysts (e.g., Shepard and Zeckhauser, 1977), were only partially aware of the mutual relevance of their methodological research.

The thrust of much of this diverse body of research is how to cope with the effects of population heterogeneity on the parameters of the process of interest. The most common conceptualization of the problem is that there is some unobserved variable that influences the likelihood that an individual will "die" at some particular time. Sometimes this variable is of direct interest; in other cases, it is essentially a nuisance. When it is of direct interest, methods to estimate parameters of its distribution, may be important. But whether it is of interest or just a nuisance, one must be concerned with its effects in order to uncover the underlying relationship between the force of "mortality" and the variables of interest.

APPENDIX

A. Proof of the Generalized Kolmogorov-Fokker-Planck Equation

Consider the random process (YxX) defined on probability space (Ω,H,P) by the relations:

$$dY(t) = (a(t,Y(t),X_0^t)\ I(t)dt + b(t,Y(t),X_0^t)\ I(t)dW_1(t),Y(0) \tag{A1}$$

and

$$dX(t) = (H(t,Y(t),X_0^t)\ I(t)dt + B(t,Y(t),X_0^t)\ I(t)dW_2(t),X(0) \tag{A2}$$

where $W_1(t)$ and $W_2(t)$ are independent Wiener processes that are also independent of the initial conditions Y(0) and X(0). Coefficients a, A, and b are measurable functions of t, Y(t), and the entire history of the process X from time 0 to time t. B is a positive, measurable function of t and the entire history of the process X. I(t) is a two state (1,0) continuous time process with I(0)=1, such that the transition intensity function

$$\tilde{\mu}(t,Y(t),X,I(t)) = \mu(t,Y(t),X)\ I(t) \tag{A3}$$

where $\tilde{\mu}(t,Y(t),X_0^t)$ is a measurable function of t, Y(t), and the entire history of the process X up to time t.

The proof of the generalized Kolmogorov-Fokker-Planck equation for the density of the unobserved variable conditional on I(t)=1 and X_0^t is based on the formula for the conditional mathematical expectation of an arbitrary, bounded, doubly differentiable function F(Y(t)). This formula may be derived as a consequence of the general estimation approach based on semimartingale theory (Jacod, 1979; Bremand, 1981), as well as the methods of filtration of random processes with jumping components (Yashin, 1969) and the analagous methods given in Liptzer and Shirjaev (1977). Here we sketch the proof.

Using Bayes' formula, one can write

$$E(f(Y(t))|I(t) = 1,\ X_0^t) = E'(F(Y(t)\cdot\ \phi(t)) \tag{A4}$$

where $\phi(t)$ is the likelihood ratio given by

$$\phi(t) = \exp\{\int_0^t \frac{A(u,Y(u),X) - \bar{A}(u,X)}{B(u,X)} d\bar{W}(a) - \tfrac{1}{2} \int_0^t \frac{(A(u,Y(u),X) - \bar{A}(u,X))^2}{B^2(u,X)} du$$

$$+ \int_0^t (\bar{\mu}(u,X) - \mu(u,Y(u),X))du \quad \text{(A5)}$$

where

$$\bar{W}(t) = \int_0^t \frac{d\, X(u) - \bar{A}(u,X)du}{B(u,X)} \quad \text{(A6)}$$

is the Wiener process with respect to the family of σ-algebras generated by the process X and where

$$\bar{A}(t,X) = E(A(t,Y(t),X_0^t)\,|\,I(t) = 1,X_0^t) \quad \text{(A7)}$$

and

$$\bar{\mu}(t,X) = E(\mu(t,Y(t),X_0^t)\,|\,I(t) = 1,X_0^t) \quad \text{(A8)}$$

The symbol E' means the operation of mathematical expectation with respect to the marginal probability measure concentrated on the component W_1 of the Wiener process.

Using Ito's differential rule (Liptser and Shirjaev, 1977), one can readily transform (A5) into the differential relationship

$$d\Phi(t) = \phi(t) \frac{A(t,Y(t),X_0^t) - \bar{A}(t,X_0^t)}{B(t,X_0^t)} d\bar{W}(t)$$

$$- (\mu(t,Y(t),X_0^t) - \bar{\mu}(t,X_0^t))dt \quad \text{(A9)}$$

In order to calculate (A4), represent the product of F(Y(t)) and $\phi(t)$ by using Ito's differential rule. This yields

$$F(Y(t))\ \Phi(t) = F(Y(0))\ \phi(0) + \int_0^t F'(Y(u))\ \phi(u)\ a(u,Y(u),X_0^t)\ du$$

$$+ \int_0^t F(Y(u))\ \Phi(u)\ \frac{A(u,Y(u),X_0^t) - \bar{A}(u,X)}{B(u,X_0^t)} d\bar{W}(u)$$

$$-(\mu(u,Y(u),X_0^t) - \bar{\mu}(u,X_0^t)du + \int_0^t F'(Y(u))\phi(u)\ b(u,Y(u),X_0^t)dW_1(u) \quad \text{(A10)}$$

$$- \tfrac{1}{2} \int_0^t F''(Y(u))\ \Phi(u)\ b^2(u,Y(u),X_0^t)\ du$$

where F' and F'' are the first and second order derivatives of F with respect to Y.

Taking the mathematical expectation E' of both sides of (A10), we get

$$\begin{aligned} E(F(Y(t))|I(t) = 1,X_0^t) = E(F(Y(0)|I(0) = 1,X_0) &+ \int_0^t E'(F'(Y(u))\ a(u,Y(u),X)\phi(u))du \\ &- \tfrac{1}{2}\int_0^t E'(F''(Y(u))\ b^2(u,Y(u),X)\ \phi(u))du \\ &- \int_0^t E'(F(Y(u))\mu(u,Y(u),X)\cdot\phi(u))du \\ &+ \int_0^t E'(F(Y(u))\ \bar{\mu}(u,X)\ \phi(u))du \\ &+ \int_0^t E'(F(\&(u))\ \phi(u)\cdot\frac{A(u,Y(u),X) - \bar{A}(u,X)}{B(u,X)})\ d\bar{W}(u). \end{aligned} \tag{A11}$$

By again using Bayes' formula one can show

$$\begin{aligned} E(F(Y(t))|I(t=1),X_0^t) &= E(F(Y(0)|I(0) = 1,X_0) \\ &+ \int_0^t E(F'(Y(u))\cdot\ a(u,Y(u),X)|I(u)=1,X_0^u)du \\ &- \tfrac{1}{2}\int_0^t E(F''(Y(u))\ B^2(u,Y(u),X)|I(u)=1,X_0^u)du \\ &+ \int_0^t E(F(Y(u))(\bar{\mu}(u,X_0^u) - \mu(u,Y(u),X))|I(u)=1,X_0^u)du \\ &+ \int_0^t E(F(Y(u))\frac{A(u,Y(u),X) - \bar{A}(u,X_0^u)}{B(u,X)}|I(u)=1,X_0^u)d\bar{W}(u). \end{aligned} \tag{A12}$$

Using the arbitrary doubly differentiable function F(Y) such that

$$F(\pm\infty) = F'(\pm\infty) = F''(\pm\infty) = 0 \tag{A13}$$

and rewriting (A12) in terms of the integral with respect to the conditional density

$$\mathcal{L}_t(y) = \frac{\partial}{\partial y} P(Y(t)\le y|I(t)=1,X_0^t) \tag{A14}$$

one can finally get the conditional Kolmogorov-Fokker-Planck equation given in the main text.

B. Proof that the Conditional Distribution is Gaussian

In order to prove that the conditional density $f_t(y)$ is Gaussian, some additional assumptions are needed. We assume that the coefficients a, A, and μ have the following forms:

$$a(u,Y(u),X_0^t) = a_0(u,X_0^t) + a_1(u,X_0^t)\ Y(u)$$

$$A(u,Y(u),X_0^t) = A_0(u,X_0^t) + A_1(u,X_0^t)\ Y(u)$$

$$\mu(u,Y(u),X_o^t) = \mu_0(u,X_0^t) + \mu_1(u,X_0^t)\ Y(u) + \mu_2(u,X_0^t)\ Y^2(u)$$

of time and of the entire past of the process X from time 0 up to time t. We assume also that the initial condition Y(0) is Gaussian distributed conditional on I(0)=1 and X_0^t,

$$F(Y(t)) = e^{i\,\alpha\,Y(t)} \tag{B2}$$

Denote by

$$\Psi_t = E(e^{i\alpha Y(t)} \,|\, I(t)=1, X_0^t) \tag{B3}$$

For this special case (A12) may be written as

$$\begin{aligned}
\Psi_t = \Psi_0 &+ i\alpha \int_0^t a_0(u,Y(u))\ \Psi_u\ du + \alpha \int_0^t \Psi'_n\ a_1(u,X)du \\
&- \frac{\alpha^2}{2} \int_0^t \Psi_u\ b^2(u,X)du + \int_0^t \mu_2(u,X)\ \Psi''_u\ du \\
&+ \int_0^t \mu_2(u,X)\ \bar{Y}^2(u)\ \Psi_u + \int_0^t \mu_1(u,X)\ m(u)\ \Psi_u\ du \\
&- i \int_0^t \mu_1(u,X)\ \Psi'_u\ du \\
&- i \int_0^t \Psi'_u \frac{A(u,X)}{B(u,X)}\ d\bar{W}(u) - \int_0^t \Psi_u\ \frac{A(u,X)\ m(u)}{B(u,X)}\ d\bar{W}(u)
\end{aligned} \tag{B4}$$

where X' and X" denote the first and second derivatives with respect to α and

$$m(t) = E(Y(t) \,|\, I(t)=1, X_0^t) \tag{B5}$$

Denote by m_0 and γ_0 the mean and variance of the conditional distribution of Y_0. Then the function Ψ_0 can be written as

$$\Psi_0 = \exp\{i\alpha m_0 - \tfrac{1}{2}\,\alpha^2\gamma_0\} \tag{B6}$$

Given this particular form and the equation for Y_t, we seek Y_t in the similar form:

$$\Psi_t = \exp\{i\alpha m(t) - \tfrac{1}{2}\,\alpha^2\gamma(t)\} \tag{B7}$$

where m_t and γ_t satisfy the following stochastic differential equations

$$dm(t) = c_1(t)\ dt + d_1(t)\ d\bar{W}(t) \tag{B8}$$

$$d\gamma(t) = C_2(t)\ dt + d_2(t)\ d\bar{W}(t)$$

The coefficients in (B8) can be found from (B1) and (B7).

Using the equalities

$$\Psi'_m = i\alpha\Psi\ \Psi''_{mm} = -\alpha^2\Psi,\ \Psi''_m\gamma = -\tfrac{1}{2}\ i\ \alpha^3\ \Psi \tag{B9}$$

$$\Psi'_\gamma = -\tfrac{1}{2}\ \Psi\ \alpha^2,\ \Psi''_{\gamma\gamma} = -\tfrac{1}{4}\ \Psi\ \alpha^4$$

and comparing the stochastic differential of Ψ_t represented in terms of m_t and γ_t with the right hand side of (B5), we have

$$C(t) = a_0(t,X) + a_1(t,X)\ m(t) - \gamma(t)(\mu_1(t,X) + \mu_2(t,X)\ m(t))$$

$$d_1(t) = \frac{A(t,X)}{B(t,X)}\ \gamma(t),\ d_2(t) \equiv 0 \tag{B10}$$

$$C_1(t) = b^2(t,X) - 2\ a_1(t,X)\ \gamma(t) - \mu(t,X)\ \gamma^2(t) - \frac{A(t,X)}{B(t,X)}\ \gamma^2(t)$$

It remains to be shown that the equation for γ_t has a unique solution. Proof of this follows easily from the approach suggested by Liptzer and Shirjaev (1977). Furthermore, generalization to the case described in Section III.C.--i.e., when noise in X and Y is correlated--also follows easily from Liptzer and Shirjaev.

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