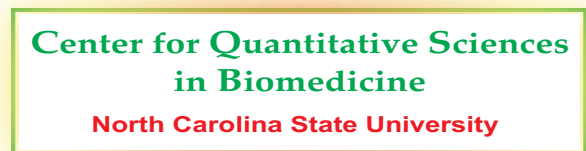


Propagation of Uncertainty in Dynamical Systems

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Propagation of Uncertainty in Dynamical Systems

- (i) Cryptodeterministic (deterministic propagation of random IC)
- (ii) Stochastic differential equations (Ito diffusion processes, Fokker-Planck)
- (iii) Random differential equations (nonlinear, nonadditive dependence on uncertainty)
 - (iiia) Distributions on parameters in deterministic dynamics (GRD)
- (iv) Individual/population modeling in hierarchial statistical framework
- (v) Probability distribution dependent dynamics

Motivating Examples: Mosquitofish and Shrimp Modeling

From joint efforts on modeling of variability in growth in shrimp populations with

V. A. Bokil, J.L. Davis, Stacey Ernstberger, Shuhua Hu (CRSC)
E. Artimovich, A. K. Dhar, R. A. Bullis, (AdvBioNutrition)
C. L. Browdy (Waddell Marine Culture Center)

Builds on interests and efforts since late 1980's on uncertainty in population modeling—mosquitofish—by HTB, F. Kappel, L. Botsford, C. Wang, B. Fitzpatrick, H. Tran, Y. Zhang, L. Potter, K. Bihari, et al.,—(Brown, USC, NCSU)

References

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- [8] HTB and S. Hu, Nonlinear stochastic Markov processes and modeling uncertainty in populations, CRSC-TR11-02, N.C. State University, Raleigh, NC, January, 2011; *Math. Biosci. Engr.*, submitted.

Shrimp Modeling: Motivation and Methods

Motivation

- Develop a stable operational platform for rapid production of large quantities of therapeutic and/or preventative countermeasures responding to bio toxic attacks on population.
- Foundation in economical platform for production of complex protein therapeutics to replace mammalian cell culture production methods used in pharmaceutical industry.

Method

- Use shrimp as scaffold organism to produce biological countermeasures.
- Recruit biochemical machinery in existing biomass for production of vaccine or antibody – infection using a virus carrying a passenger gene for desired countermeasure.

Penaeus Vannamei Shrimp



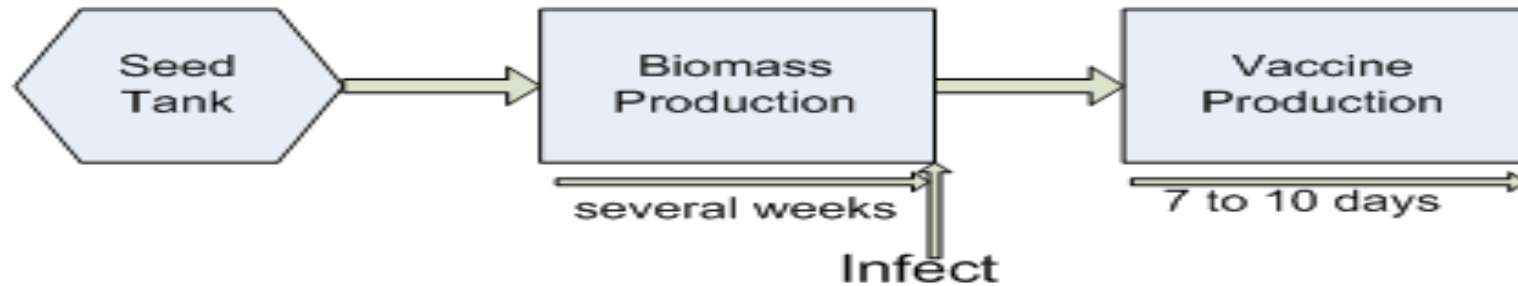
Biosecure Shrimp Production System at Waddell Marine Culture Center



Hybrid Model of Shrimp Biomass/Vaccine Production System

Model Components

- Simulating biomass production model over some time interval.
- Feeding the output of biomass production model to the input of vaccine production model.



Biomass Production Model

Production System

- Size dependent characteristics.

Size-Structured Population Model (Sinko-Streifer)

$$u_t + (g(x, t)u)_x + m(x, t)u = 0 \quad (x, t) \in (0, x_{\max}] \times (0, T],$$

$$u(0, t) = 0, \quad t \in (0, T],$$

$$u(x, 0) = u^0(x), \quad x \in [0, x_{\max}].$$

where $u(x, t)$ = density of individuals of size x in gms at time t (number per unit mass), $g(x, t) = \frac{dx}{dt}$ = growth rate of individuals of size x at time t (mass per unit time), $m(x, t)$ = mortality rate of individuals of size x at time t (per unit time).

Some Conclusions and Needed Research Directions

- Need to develop a mathematical sensitivity analysis methodology for distributions, e.g., in a Prohorov metric framework or similar topology for distributions, to aid in optimal harvest of vaccines, pharmaceuticals, etc.
- Developing an inverse problem methodology to estimate some critical parameters once we obtain the data from the experiments (need for design of experiments).
- Need for stochasticity/uncertainty in the model.

- Not just population growth models in biosciences—wide applicability to “class structured” modeling (CRD=class rate distribution models), including complex nodal network models (network security, logistics, intensity levels in nodal proliferation), general hyperbolic transport systems including CFSE label intensity in cell proliferation, etc., with inherent uncertainties or general physical systems leading to Fokker-Planck, Forward Kolmogorov systems-
- Describe ideas here in terms of population growth rate (GRD=growth rate distribution) models from shrimp problem

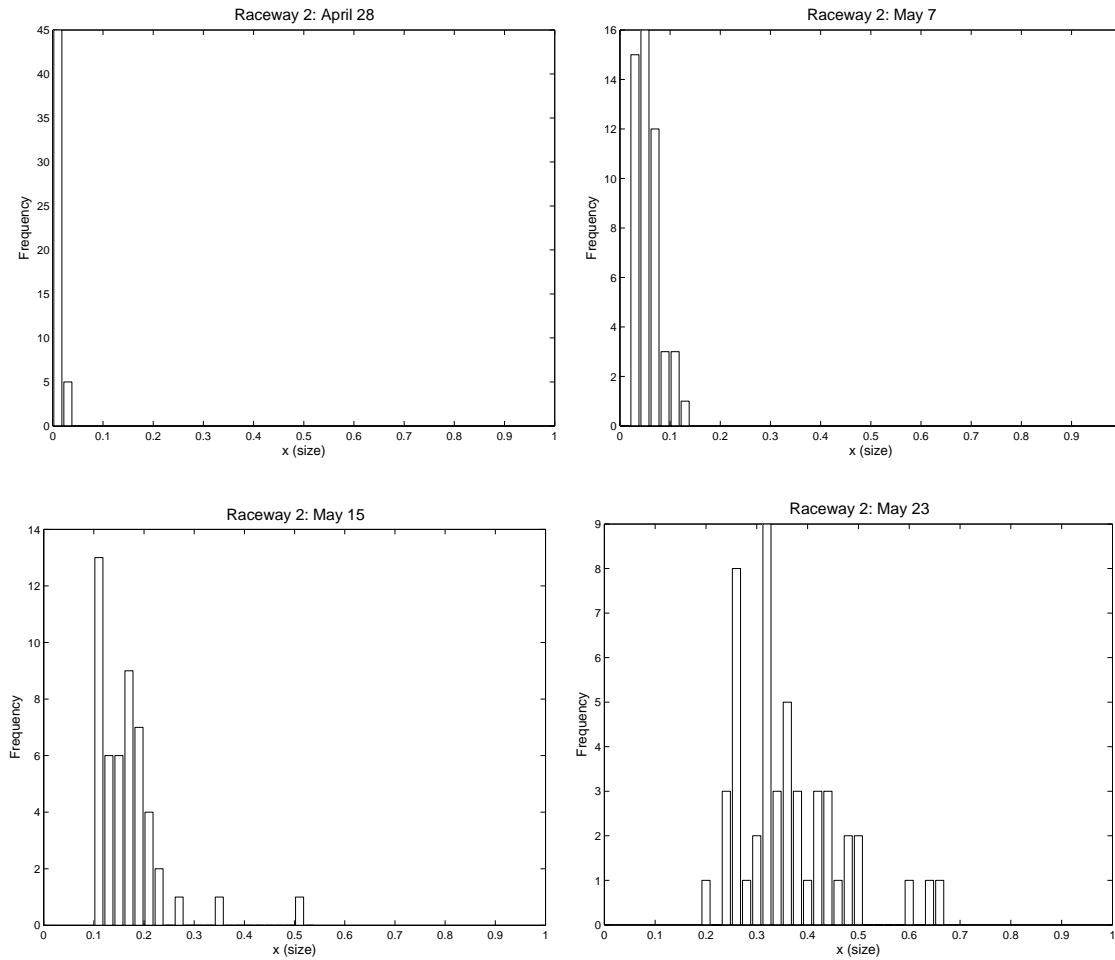


Figure 1: Histograms for longitudinal data for Raceway 2. Need for stochasticity/uncertainty in the model.

Modeling Growth Uncertainty and Variability: Probabilistic and Stochastic Formulations

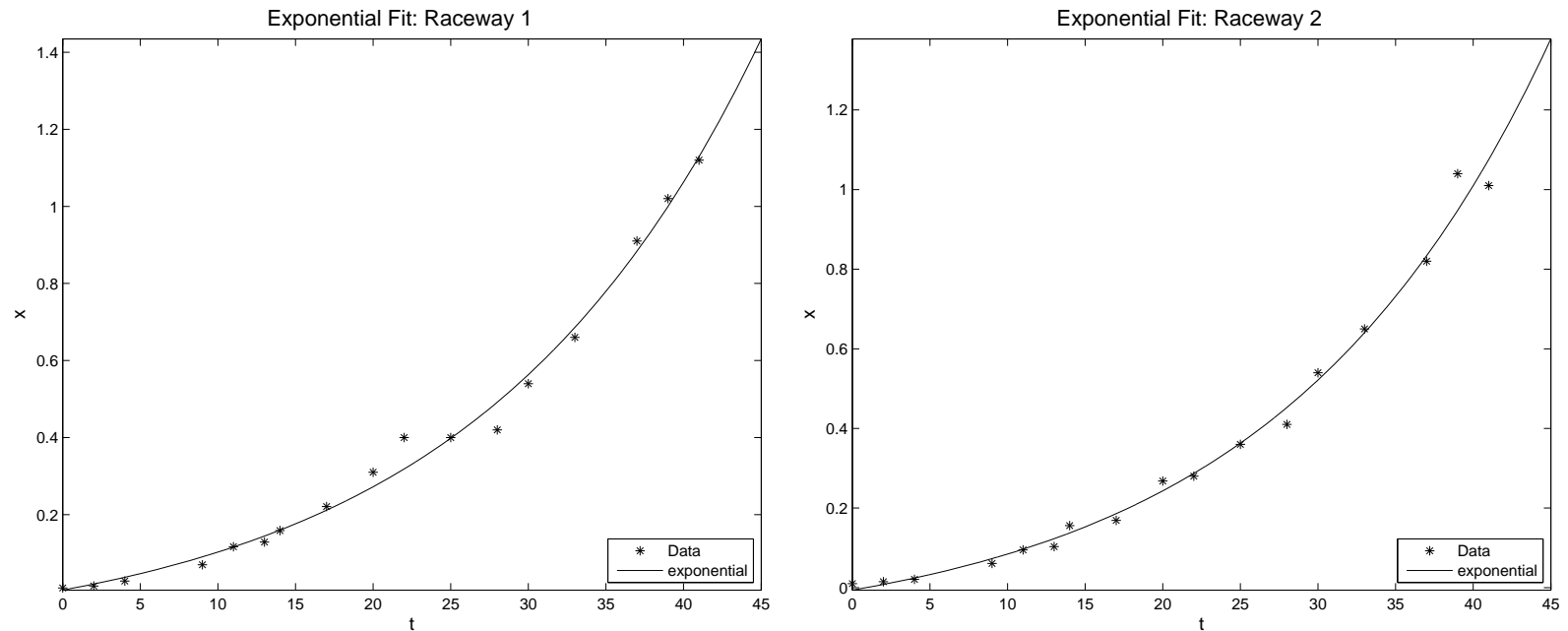


Figure 2: (left): Exponential fit of Raceway 1 data with $g(\bar{x}) = 0.054(\bar{x} + 0.133)$; (right): Exponential fit of Raceway 2 data with $g(\bar{x}) = 0.056(\bar{x} + 0.126)$.

The plots reveal that exponential functions appear to fit the data in each of the raceways. Hence, the corresponding differential equation

$$\frac{d\bar{x}}{dt} = g(\bar{x}) = b_0(\bar{x} + c_0) \quad (1)$$

is a reasonable description of the early growth of shrimp. Here b_0 is a positive constant which denotes the **intrinsic growth rate**, and c_0 is a positive constant which we shall refer to as the **affine growth term**.

Let $X(t)$ = a **random variable** which we use to denote the **size of an individual** in the population at time t . That is, each realization corresponds to the size at time t of an individual. Then we can write an analogue of (1) for **mean growth dynamics** as

$$\frac{dE(X(t))}{dt} = b_0(E(X(t)) + c_0). \quad (2)$$

Note that

$$\frac{dx}{dt} = g(x) = b(x + c), \quad x(0) = x_0 \quad (3)$$

has solution

$$x(t) = x_0 \exp(bt) + c\{\exp(bt) - 1\}. \quad (4)$$

If $x_0 = X_0$ is random, then obtain cryptodeterministic model for stochastic size process

$$X(t) = X_0 \exp(bt) + c\{\exp(bt) - 1\}, \quad (5)$$

with $E(X(t))$ satisfying expected mean growth dynamics

$$\frac{dE(X(t))}{dt} = b(E(X_0) + c) \exp(bt) = b(E(X(t)) + c). \quad (6)$$

In this formulation the size random variable $X(t)$ has variance

$$\text{Var}(X(t)) = \exp(2bt)\text{Var}(X_0). \quad (7)$$

IMPLICATIONS:

Little to no dispersion in size if $\text{Var}(X_0) \approx 0$ (i.e., all shrimp initially approximately the same size)

But data suggests **significant dispersion** in size from approximately no variance in initial sizes!!!

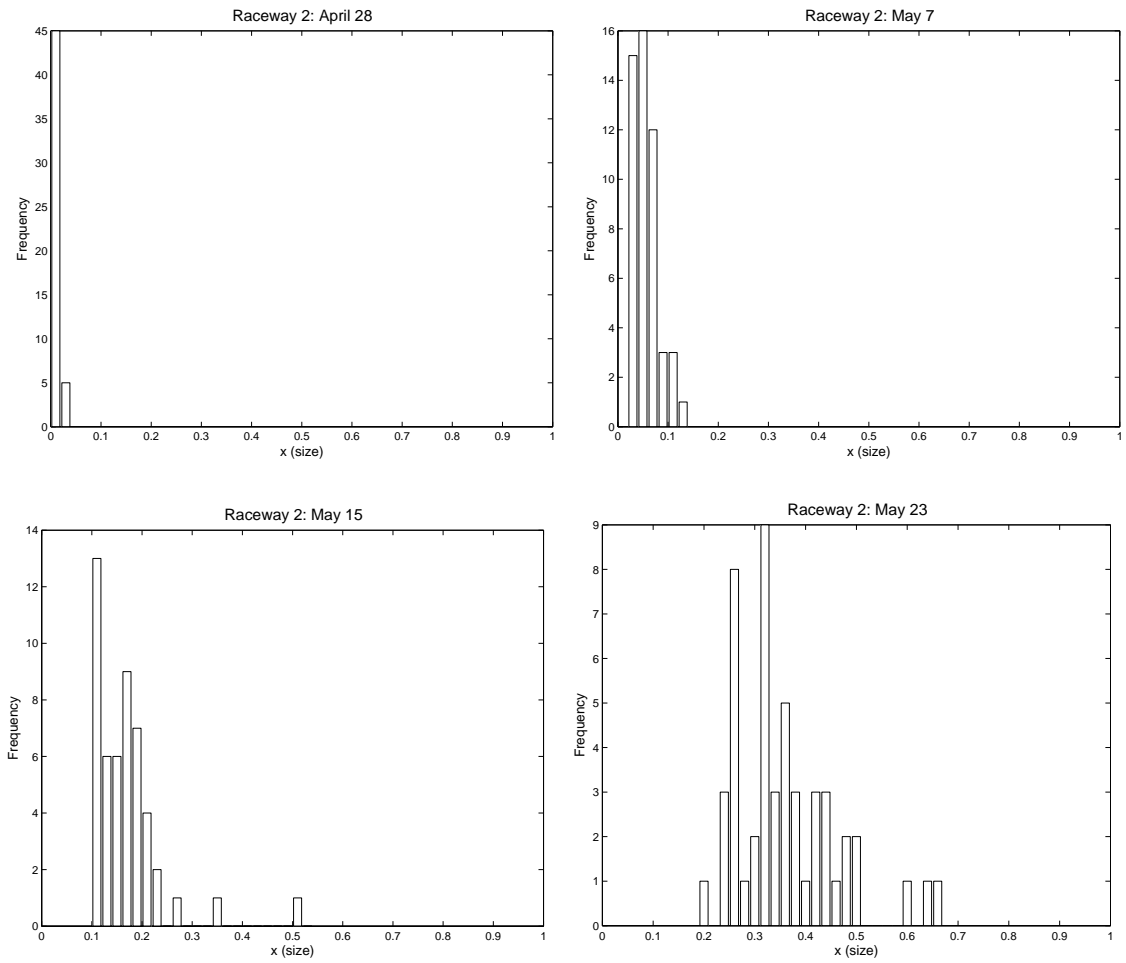


Figure 3: Histograms for longitudinal data for Raceway 2.

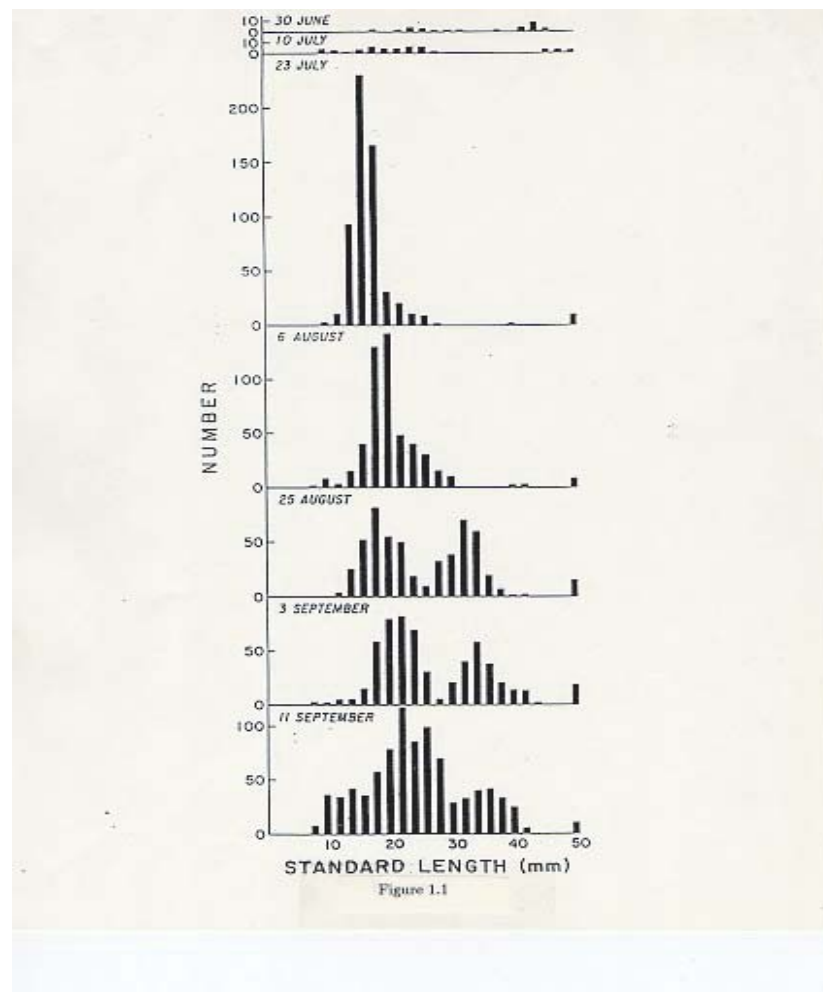


Figure 4: Histograms for mosquitofish data.

Probabilistic vs. Stochastic Formulations

1 Probabilistic Approach

- assume each individual grows according to a deterministic growth model, but different individuals (even of the same size) may have different size dependent growth rates.
- partition the entire population into (possibly a continuum of) subpopulations where individuals in each subpopulation have the same growth rate.
- assign a probability distribution to this partition of possible growth rates in the population. The growth process for individuals in a subpopulation with the rate g is described by the model

$$\frac{dx(t; g)}{dt} = g(x(t; g), t), \quad g \in \mathcal{G}, \quad (8)$$

where \mathcal{G} is the collection of admissible growth rates.

Thus **growth uncertainty** introduced into population by the variability of growth rates among subpopulations of individuals—corresponding phenomenon may be attributed to the effect of genetic differences or some chronic disease on the growth of individuals. With this assumption of a family of admissible growth rates and an associated probability distribution, one thus obtains a generalization of the Sinko-Streifer model, called the **Sinko-Streifer Growth Rate Distribution (SSGRD) model**, which has been formulated and studied in Banks-Botsford-Kappel-Wang, 1987; Banks-Fitzpatrick, 1991.

The model consists of solving

$$\begin{aligned}
 v_t(x, t; g) + (g(x, t)v(x, t; g))_x &= 0, \\
 v(0, t; g) &= 0, v(x, 0; g) = v_0(x; g),
 \end{aligned}
 \tag{9}$$

for a given $g \in \mathcal{G}$ and then “summing” (with respect to the probability) the corresponding solutions over all $g \in \mathcal{G}$. Thus if $v(x, t; g)$ is the population density of individuals with size x at time t having growth rate g , the expectation of the total population density for size x at time t is given by

$$u(x, t) = \int_{g \in \mathcal{G}} v(x, t; g) d\mathcal{P}(g), \quad (10)$$

where \mathcal{P} is the probability measure on \mathcal{G} . This probabilistic structure \mathcal{P} on \mathcal{G} is then the fundamental “parameter” to be determined from aggregate data for the population. Thus this *probabilistic formulation* involves a

stationary probabilistic structure

on a

family of deterministic dynamical systems.

2 Stochastic Formulation

An alternative formulation—based on assumption that movement from one size class to another can be described by a stochastic diffusion process. Let $X(t)$ be a Markov diffusion process which represents size at time t . Then $X(t)$ is described by the Ito stochastic differential equation (we refer to this equation as the stochastic growth model)

$$dX(t) = g(X(t), t)dt + \sigma(X(t), t)dW(t), \quad (11)$$

where $W(t)$ = standard Wiener process. Here $g(x, t)$ = average or mean growth rate of individuals with size x at time t , and is given by

$$\lim_{\Delta t \rightarrow 0^+} \frac{1}{\Delta t} \mathbf{E}(\Delta X(t) | X(t) = x) = g(x, t), \quad (12)$$

where $\Delta X(t) = X(t + \Delta t) - X(t)$.

The function $\sigma(x, t)$ represents variability in growth rate of individuals – given by

$$\lim_{\Delta t \rightarrow 0^+} \frac{1}{\Delta t} \mathbf{E}([\Delta X(t)]^2 | X(t) = x) = \sigma^2(x, t). \quad (13)$$

- Growth process for each individual is stochastic—each individual grows according to stochastic growth model (11).
- Individuals with same size at same time have same variability in the growth. Thus, growth uncertainty/variability is introduced into population by growth stochasticity of each individual.
- Phenomenon might be explained in some situations by influence of fluctuations of environment on growth rate of individuals, e.g., growth rate of shrimp affected by temperature, salinity, dissolved oxygen level, un-ionized ammonia level, etc.

This assumption on growth process leads to **Fokker-Planck (FP)** or **forward Kolmogorov model** for population density u , (carefully derived by **Okubo** among numerous others and subsequently studied in many references (e.g., **L. Allen, Banks-Tran-Woodard, T. Gard**)). The equation with appropriate boundary conditions is given by

$$\begin{aligned}
 u_t(x, t) + (g(x, t)u(x, t))_x &= \frac{1}{2}(\sigma^2(x, t)u(x, t))_{xx}, & u(x, 0) &= u_0(x), \\
 g(0, t)u(0, t) - \frac{1}{2}(\sigma^2(x, t)u(x, t))_x|_{x=0} &= 0, \\
 g(L, t)u(L, t) - \frac{1}{2}(\sigma^2(x, t)u(x, t))_x|_{x=L} &= 0.
 \end{aligned}
 \tag{14}$$

More generally:

$$g(0, t)u(0, t) - \frac{1}{2}(\sigma^2(x, t)u(x, t))_x|_{x=0} = \int_0^L \beta(\xi, t)u(\xi, t)d\xi \tag{15}$$

Note $\sigma = 0$ in FP yields SS (no variance in growth rate) so SS is deterministic version for size densities.

Comparison of deterministic (SS) vs. stochastic growth (FP)

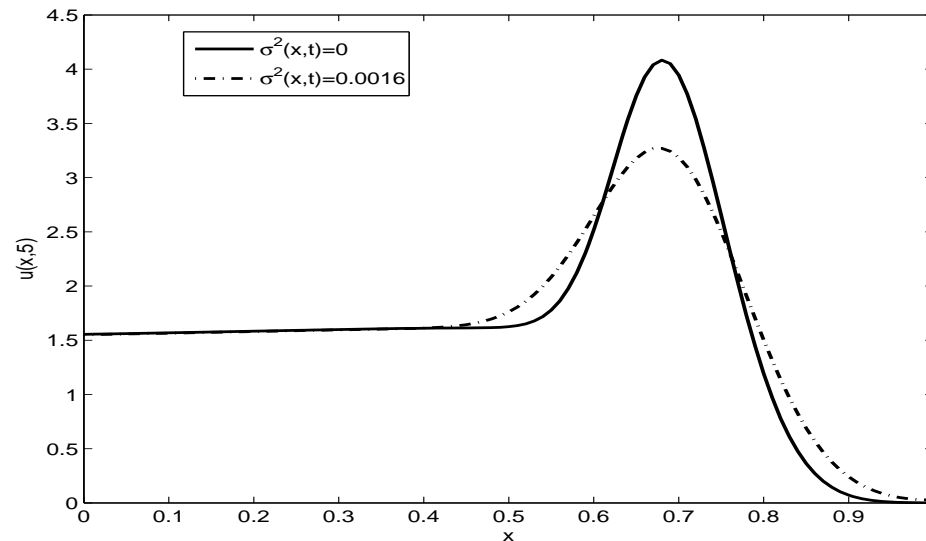


Figure 5: Population density as a function of size x at time $t = 5$ for $\sigma = 0$ vs. $\sigma = .04$. Parameters: $g(x) = .2(1 - x)$, $m = .3$, $\beta(x) = .2 \exp(-(x - .5)^2)$

Modeling Summary

From above discussions, we readily see

- In probabilistic structure formulation resulting in the SSGRD model, the growth of each individual is a **deterministic process**.
- In stochastic formulation, growth of each individual is a **stochastic process** resulting in the FP model.
- Hence, these two formulations are **conceptually quite different**.
- Choice of formulation to describe the dynamics of a particular population should, **if possible**, be based on the mechanisms and/or scenarios that are the primary sources of the uncertainty/variability in growth.

SUBSEQUENT EFFORTS INCLUDE:

- Development of experiments at ABN, Waddell Center, and Oceanic Institute to determine variability in growth, mortality, to “validate” Sinko-Streifer Growth Rate Distribution or to investigate need for Fokker-Planck vs. Sinko-Streifer GRD. Experiments were designed using math models and simulations for inverse problems (how much data?? how often??). Experiments designed and carried out in Winter, 2007-2008.
- Compare Fokker-Planck with SS Growth Rate Distribution models to determine best way to include uncertainty/stochasticity. Question: How to put comparable amounts of uncertainty in each of probabilistic and stochastic formulations to make reasonable comparisons ?????

IF SSGRD generates a stochastic process for size(???), could then match up means and variances of each process!!

IDEA: Put distribution on \mathbf{b} , \mathbf{c} , and \mathbf{x}_0 simultaneously in $g(\mathbf{x}) = \mathbf{b}(\mathbf{x} + \mathbf{c})$ in the deterministic system

$$\frac{d\mathbf{x}(t)}{dt} = \mathbf{b}(\mathbf{x} + \mathbf{c}), \quad \mathbf{x}(0) = \mathbf{x}_0. \quad (16)$$

More generally, using the solution

$$\mathbf{x}(t; \mathbf{b}, \mathbf{c}, \mathbf{x}_0) = (\mathbf{x}_0 + \mathbf{c}) \exp(\mathbf{b}t) - \mathbf{c}, \quad (17)$$

of (16) and assuming that \mathbf{B} , \mathbf{C} and \mathbf{X}_0 are random variables for \mathbf{b} , \mathbf{c} and \mathbf{x}_0 , respectively, we can always define a stochastic process

$$\mathbf{X}(t; \mathbf{B}, \mathbf{C}, \mathbf{X}_0) = (\mathbf{X}_0 + \mathbf{C}) \exp(\mathbf{B}t) - \mathbf{C}, \quad (18)$$

and argue that it satisfies the random differential equation

$$\frac{d\mathbf{X}(t)}{dt} = \mathbf{B}(\mathbf{X}(t) + \mathbf{C}), \quad \mathbf{X}(0) = \mathbf{X}_0. \quad (19)$$

But in general one **cannot say anything** about $E(\mathbf{X}(t))$ and $\text{Var}(\mathbf{X}(t))$ without special assumptions on \mathbf{B} , \mathbf{C} and \mathbf{X}_0 that would enable one to ascertain statistical properties of $\mathbf{X}(t)$ and statistical relationships between $\mathbf{X}(t)$, \mathbf{B} , \mathbf{X}_0 and \mathbf{C} .

However, if \mathbf{C} is constant and \mathbf{B} assumed normal and independent of \mathbf{X}_0 , then can find distribution for stochastic process defined by (18).

Need result (one in a class of transformation theorems for RVs):

Lemma 1. *If $\ln Z \sim \mathcal{N}(\mu, \sigma^2)$, then Z is log-normally distributed, where its probability density function $f_Z(z)$ is defined by*

$$f_Z(z) = \frac{1}{z\sqrt{2\pi}\sigma} \exp\left(-\frac{(\ln z - \mu)^2}{2\sigma^2}\right),$$

and its mean and variance are given by

$$E(Z) = \exp\left(\mu + \frac{1}{2}\sigma^2\right), \quad \text{Var}(Z) = [\exp(\sigma^2) - 1] \exp(2\mu + \sigma^2).$$

$\implies Y(t) \equiv \exp(Bt)$ is log normal if $B \sim \mathcal{N}$

THEORY:

Can prove (theorems!!) that the **size distribution** (probability density function for $X(t)$) obtained from the stochastic formulation is exactly the same as that obtained from probabilistic formulation (as long as their initial size distributions $X(0)$ are the same (either deterministic or random)) in several cases of interest:

EXAMPLE 1 (MGD):

Stochastic formulation:
$$dX(t) = b_0(X(t) + c_0)dt + \sqrt{2t}\sigma_0(X(t) + c_0)dW(t)$$

Probabilistic formulation:
$$\frac{dx(t;b)}{dt} = (b - \sigma_0^2 t)(x(t;b) + c_0), b \in \mathbb{R}$$

with $B \sim \mathcal{N}(b_0, \sigma_0^2)$,

EXAMPLE 2 (NO MGD):

Stochastic formulation:
$$dX(t) = (b_0 + \sigma_0^2 t)(X(t) + c_0)dt + \sqrt{2t}\sigma_0(X(t) + c_0)dW(t)$$

Probabilistic formulation:
$$\frac{dx(t;b)}{dt} = b(x(t;b) + c_0), b \in \mathbb{R}$$

with $B \sim \mathcal{N}(b_0, \sigma_0^2)$,

REMARK: Example 1 satisfies mean growth dynamics (MGD)

$$\frac{d\mathbb{E}(X(t))}{dt} = b_0(\mathbb{E}(X(t)) + c_0)$$

while Example 2 does not. Both models reduce to deterministic affine growth rate model $\dot{x} = b_0(x + c_0)$ when $\sigma_0 = 0$.

COMPUTATION:

- Practical problem: in probabilistic formulation, normal distribution $\mathcal{N}(b_0, \sigma_0^2)$ for B not completely reasonable—the intrinsic growth rate b can be negative—results in the size having non-negligible probability of being negative in a finite time period when σ_0 sufficiently large compared to b_0 .
- Typical (and reasonable) fix-up: impose a truncated normal distribution $\mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2)$ instead of normal distribution, i.e., restrict B to some reasonable range $[\underline{b}, \bar{b}]$.
- Stochastic formulation can also lead to the size having non-negligible probability being negative when σ_0 is sufficiently large compared to b_0 : $W(t) \sim \mathcal{N}(0, t)$ for any fixed t . Possible remedy: set $X(t) = 0$ if computed $X(t) \leq 0$.

IN SUMMARY: If σ_0 is large compared to b_0 , may obtain different size distributions for these two formulations after making these different modifications.

HERE: Give numerical examples to illustrate difficulties and possible resolutions—demonstrate how solutions to FP model and SSGRD model change as we vary the values of σ_0 and \underline{b} .

Numerical Results

- Time interval $t \in [0, 10]$
- Initial conditions FP:

$$u_0(x) = 100 \exp(-100(x - 0.4)^2)$$

- Initial Conditions GRD:

$$v_0(x; b) = 100 \exp(-100(x - 0.4)^2) \quad \text{for } b \in [\underline{b}, \bar{b}]$$

$$c_0 = 0.1, b_0 = 0.045, \quad \sigma_0 = rb_0, \quad r > 0.$$

- Use $\Delta x = 10^{-3}$ and $\Delta t = 10^{-3}$ in finite difference scheme to numerically solve FP model.
- In both examples, vary values of r and \underline{b} to see effect on solutions to FP and GRD

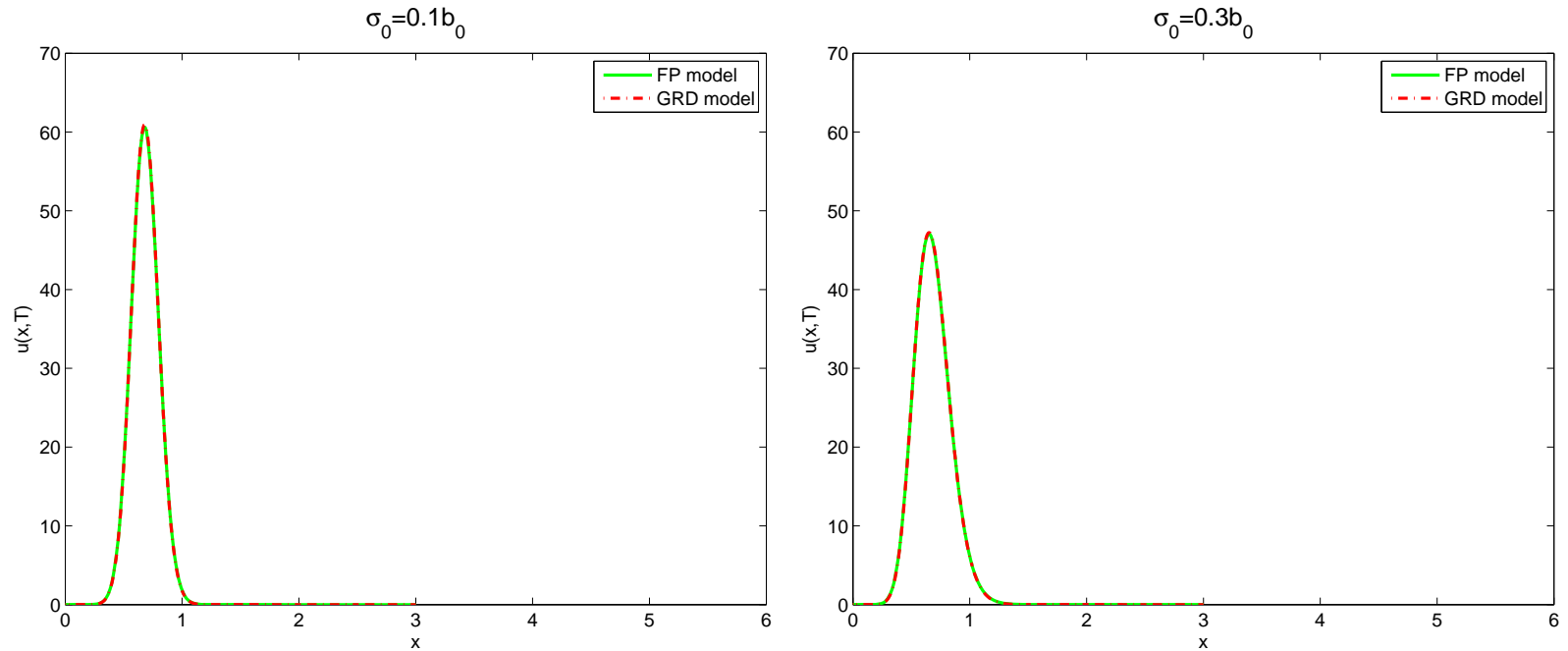
Example 1: Parameters:

FP model: $g(x) = b_0(x + c_0)$, $\sigma(x, t) = \sqrt{2t}\sigma_0(x + c_0)$

GRD model: $g(x, t; b) = (b - \sigma_0^2 t)(x + c_0)$,

where $b \in [\underline{b}, \bar{b}]$ with $B \sim \mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2)$.

- Take $\underline{b} = b_0 - 3\sigma_0$ and $\bar{b} = b_0 + 3\sigma_0$ (so 99.7%)
- Take $r_0 = \frac{-3 + \sqrt{4b_0T + 9}}{2b_0T}$ (≈ 0.3182)
- $r < r_0 \implies g(x, t; b) > 0$ in $\{(x, t) | (x, t) \in [0, L] \times [0, T]\}$ for all $b \in [\underline{b}, \bar{b}]$, $L=3$.



Numerical solutions $u(x, T)$ for Example 1, $r = 0.1, 0.3$.

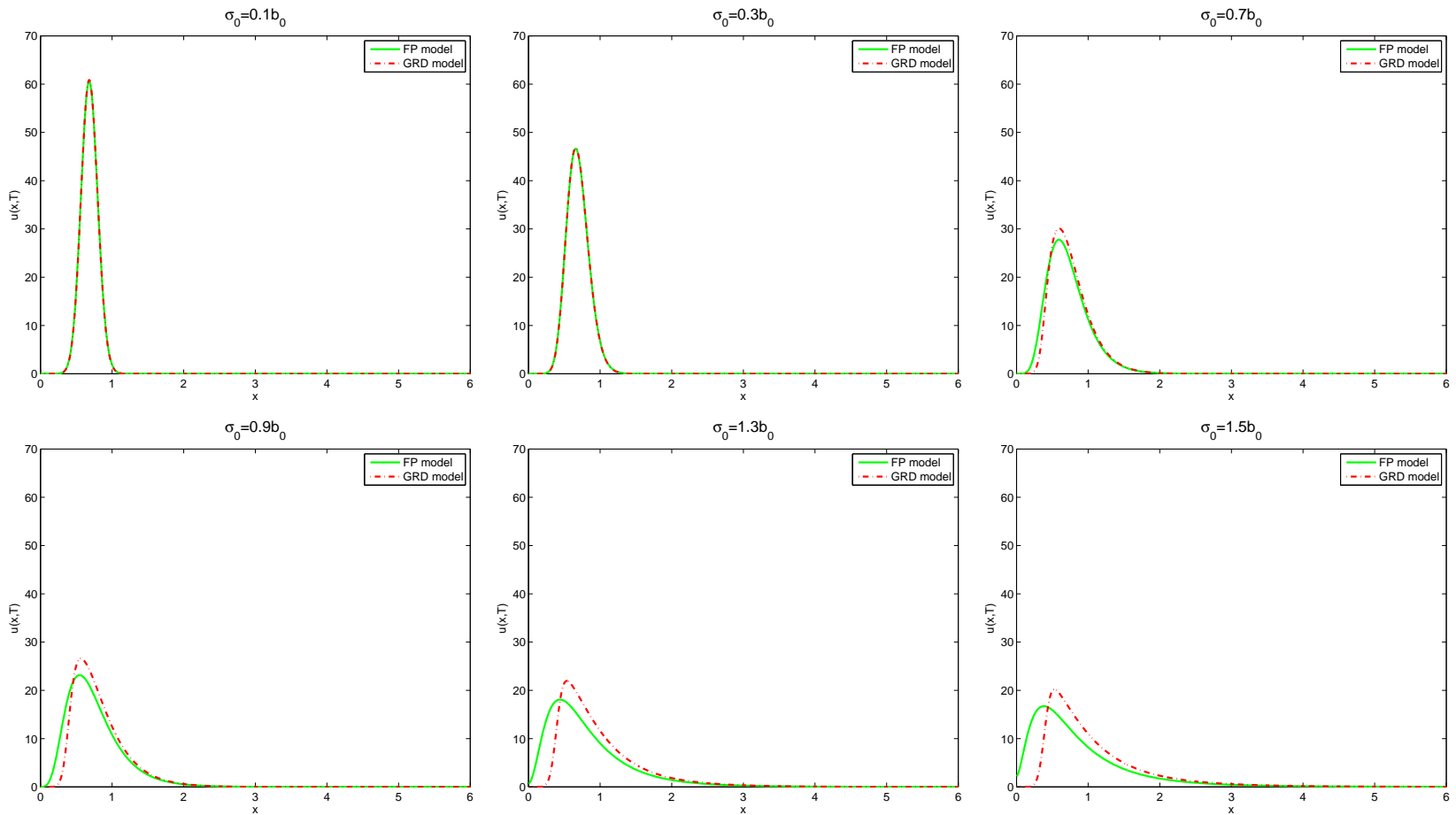
- Good approximations: $\mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2)$ good approximation of $\mathcal{N}(b_0, \sigma_0^2)$
- resulting size distribution a good approximation of theoretical size distributions obtained by GRD model and FP model

Example 2: Parameters:

$$\text{FP model: } g(x, t) = (b_0 + \sigma_0^2 t)(x + c_0), \quad \sigma(x, t) = \sqrt{2t}\sigma_0(x + c_0)$$

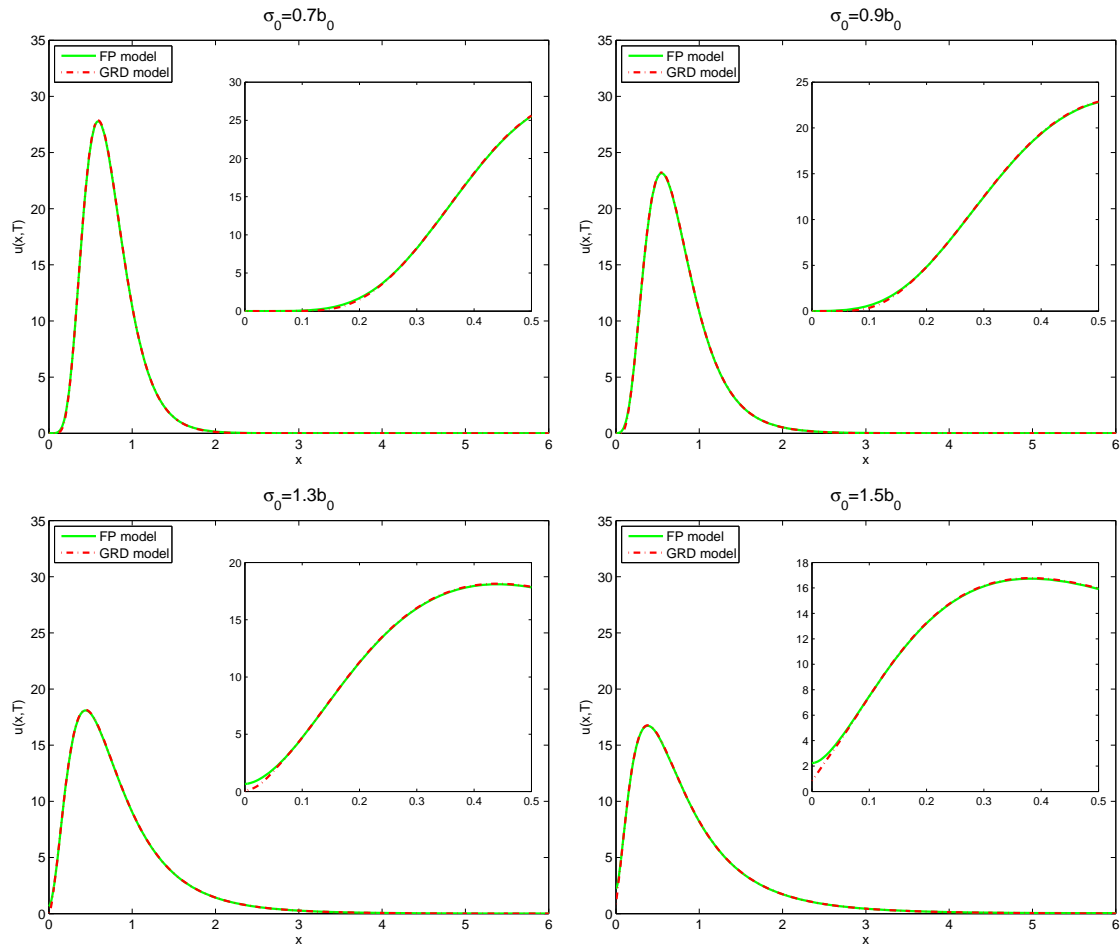
$$\text{GRD model: } g(x; b) = b(x + c_0), b \in [\underline{b}, \bar{b}], B \sim \mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2).$$

Numerical solutions of F-P and of GRD model at $t = T$ with $r = 0.1, 0.3, 0.7, 0.9, 1.3$ and 1.5 .



Numerical solutions $u(x, T)$ for Example 2: $\underline{b} = \max\{b_0 - 3\sigma_0, 10^{-6}\}$
and $\bar{b} = b_0 + 3\sigma_0$.

- $r \leq r_0 = \frac{b_0 - 10^{-6}}{3b_0} (\approx 0.3333) \implies \mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2)$ a good approximation of $\mathcal{N}(b_0, \sigma_0^2)$ Figure above: quite similar solutions for two models for $r = 0.1$ and 0.3
- But for $r > r_0$, the two solutions begin to diverge further as r increases: reason $\mathcal{N}_{[\underline{b}, \bar{b}]}(b_0, \sigma_0^2)$ is not a good approximation of $\mathcal{N}(b_0, \sigma_0^2)$ as $\underline{b} = 10^{-6}$
- FP size distribution obtained in these cases *NOT* a good approximation of size distribution obtained by GRD model anymore.
- For FP model with $r > r_0$, there exist non-negligible fraction of individuals whose size is decreased, while for GRD model size of each individual always increases as b is always positive.



Numerical solutions $u(x, T)$ with $r = 0.7, 0.9, 1.3$ and 1.5 : Example 2 with $\underline{b} = b_0 - 3\sigma_0$ and $\bar{b} = b_0 + 3\sigma_0$. Snapshot is the region $[0, 0.5]$.

- $r > 1/3$ implies existence of subpopulations in GRD model with negative growth rates—individuals in these subpopulations continue to lose weight—removed from system once size is less than zero—if situation occurs, total number of population not conserved—worse as r increases.
- For FP model, total number of population always conserved—zero-flux boundary conditions. Once size of individuals decreased to minimum size, either stay there or increase size.
- Two models yield similar solution with $r = 0.7$ and 0.9 — r not sufficiently large, size has negligible probability of being negative—most in GRD model stay in system.
- Solutions to FP and GRD models diverge (at the left part) for cases $r = 1.3$ and 1.5 —size has non-negligible probability being negative—individuals with negative size in GRD model removed

SUMMARY AND FURTHER EFFORTS

- Fokker-Planck ubiquitous in math, physics, biology, etc
- FP notoriously difficult computationally for most cases of interest
- Study further transformations for equivalence of SSGRD and FP formulations in *HTB and S. Hu, Nonlinear stochastic Markov processes and modeling uncertainty in populations, CRSC-TR11-02, N.C. State University, Raleigh, NC, January, 2011; Math. Biosci. Engr., submitted.*
- SSGRD important as alternative to computationally expensive FP, especially in inverse problems (parameter estimation for g and σ)

FURTHER CONNECTIONS: SDE, RDE, and the PROBABILISTIC FORMULATION

K. Huang, *Statistical Mechanics*, J. Wiley & Sons, New York, 1963.

Consider ensemble of particles (gas dynamics)–Positions $x(t)$ give rise to stochastic process $X(t)$ due to random velocity g in

$$\frac{dx}{dt}(t) = g(t, x),$$

which are thus realizations of $\frac{dX}{dt}(t) = G(t, X(t))$. Conservation laws result in *Liouville's equation* for probability density $\rho = \rho(t, x)$ of X :

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (g\rho) = 0 \tag{20}$$

or in scalar case

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(g\rho) = 0 \quad (21)$$

which is precisely the Sinko-Strieffer equation discussed above

$$\frac{\partial v}{\partial t} + \frac{\partial}{\partial x}(gv) = 0 \quad (22)$$

with zero mortality (conservation), where g is the individual growth rate $\frac{dx}{dt} = g(t, x)$.

The theory of RDE can then be used to make the connection between these formulations.

T.T. Soong, *Random Differential Equations in Science and Engineering*, Academic Press, New York, 1973.

Consider the Random Differential Equation

$$\frac{dX}{dt}(t) = G(t, X(t)), \quad X(0) = X_0, \quad (23)$$

where X_0 , G are independent random variables with G having probability distribution P on set \mathcal{G} of possible choices for g . Then basic result is: the probability density u for X is given by

$$u(t, x) = \int_{\mathcal{G}} v(t, x; g) dP(g) \quad (24)$$

where v is the solution of (22). This along with the relationships between the Prohorov based Probabilistic Formulation and SDEs yields a connection between certain RDE and FDE and the Probabilistic Formulation.