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STEM Degrees: **STEM Participants:**

Major Goals: We investigated two complementary topics: how living things respond to stochasticity and how we as modelers do the same. In particular, we examined the strategies organsism use for maintaining and enhancing function in unpredictable environments, and the strategies used to model complexity in the face of stochasticity.

Accomplishments: Through extensive review and synthesis of the literature, we developed the first comprehensive outline of the theme of stochastic dynamics in biological systems. Our literature review and framework provides the foundation for a review paper. We here present our detailed outline of this work and a selected bibliography of papers we synthesized.

A. Deterministic vs. stochastic processes in biological systems

i. Broad examples of mechanisms dominated by deterministic processes
ii. Broad counter-examples of mechanisms in which stochasticity plays an important role
iii. Challenges to expanding our view of the world to include stochasticity and why doing so is vitally important.
iv. Brief description of the role of math modeling in understanding biological systems.

B. Coping with stochasticity

i. Scales of stochasticity: noise vs catastrophic events
ii. Realized overcapacity: Lung tissues, genetic redundancy/degeneracy, futile cycling, large broods.
iii. Potential overcapacity:
iv. Dangers of overcapacity:

C. Capitalizing on stochasticity

i. Trial and Error (Developmental Selection): neural Development, angiogenesis, oogenesis, T cells, Rag transposons/affinity maturation.
ii. Genetic Regulation: delayed reinitiation (ATF4), gene duplication(K3L),
iii. Ploidy Changes: liver, fungi, C. neoformans

iv. Resource Acquisition: ant foraging
v. Noise in protein production: peptide fragments as an immune signal
vi. Binding Promiscuity: detoxification and immune response

D. Communication in a stochastic world

i. Stochastically established coordination: Neural growth
ii. Regulation of capacity
iii. Recognition of environmental state
iv. Robustness: maintaining a phenotype despite environmental/cellular stochasticity
v. Stochastically established coordination: immune system

E. The role of mathematical modeling in understanding stochastically driven systems

i. History and classic examples
ii. Challenges in determining when and how to use stochastic modeling
iii. Call for future work

Training Opportunities: Two graduate students were trained. Laura Strube greatly advanced her thesis work on the integrated stress response in cells, and will be completing her dissertation in October 2018 based on that research. Emerson Arehart used this opportunity to build his knowledge of complex systems and will be writing a thesis proposal based on that work to be defended in September, 2018.

Results Dissemination: Nothing to Report

Honors and Awards: Nothing to Report

Protocol Activity Status:

Technology Transfer: Nothing to Report

PARTICIPANTS:

Participant Type: PD/PI
Participant: Frederick R Adler
Person Months Worked: 6.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
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Participant Type: Graduate Student (research assistant)
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Statement of the problem studied

We investigated two complementary topics: how living things respond to stochasticity and how we as modelers do the same. In particular, we examined the strategies organsism use for maintaining and enhancing function in unpredictable environments, and the strategies used to model complexity in the face of stochasticity.

Summary of the most important results

Through extensive review and synthesis of the literature, we developed the first comprehensive outline of the theme of stochastic dynamics in biological systems. Our literature review and framework provides the foundation for a review paper. We here present our detailed outline of this work and a selected bibliography of papers we synthesized.

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