Selected Topics in Biomathematics: Applications to Ecology and Aging
Sujets choisis en biomathématiques : applications relatives à l'écologie et au vieillissement
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JOE APALOO, St. Francis Xavier University
Evolutionary Stability in Ecological Populations

Ever since Maynard Smith and Price's (1973) pioneering work, evolutionary game theory has advanced from matrix to continuous games, from single to multiple species, from scalar to vector-valued strategies, and from static analyses to adaptive dynamics. This journey made by many contributors has spawned a multitude of evolutionary stability concepts. Essentially three related stability concepts underlie the theory for predicting the outcomes of natural selection: ESS, convergence stability and NIS. The ESS concept is associated with strategies that cannot be invaded by rare alternative strategies. Convergence stability is associated with strategies that will progressively be approached under natural selection. The NIS concept is associated with strategies that can invade any nearby resident strategy. Here, we use the fitness generating function concept (G -function) and adaptive landscapes to illustrate these stability concepts. The G-function permits us to see both dynamics explicitly. The height of the adaptive landscape determines whether a given strategy would produce positive or negative population growth, and the slope of the landscape determines the selection pressure on any given strategy. Each stability concept manifests as particular configurations of the landscape. We conclude by tabulating how most of the evolutionary stability acronyms, definitions and terminologies reduce to one or several aspects of ESS, convergence stability and NIS.

JOSHUA ARMSTRONG, Dalhousie University
Application of three data mining and machine learning methods in data from the Honolulu-Asian Aging Study

As the population of older adults continues to expand across the globe, health care systems will face patient populations that are increasingly complex and difficult to manage. The challenges involved in caring for older individuals arise due to an increased number of health deficits that commonly accumulate with age. In order to better understand the accumulation of health deficits in aging populations, data mining and machine learning methods can be applied to detect previously unidentified patterns in clinical characteristics collected in longitudinal studies of aging. In a secondary analysis of data from the Honolulu-Asian Aging Study, accumulation of deficits frailty index (FI) scores were calculated for 3651 men, aged 71-93. This presentation will examine these accumulated deficits and illustrate three methods: (1) K-means clustering, (2) association rule mining (apriori algorithm), and (3) Random forests. Cluster analyses focused on identifying common patterns of deficits for the frailest individuals (FI¿0.35). Association rule mining, also known as market basket analysis, was applied to identify the most common combinations of deficits found in this sample of older men. Using data collected on these men 30 years previously, mid-life characteristics associated with fitness (low level of frailty: FI¡0.10) were identified and ranked using the Random forest algorithm. While novel exploratory methods should not replace the traditional statistical techniques that are frequently used in health research, data mining and machine learning methods should be developed for use in health data as they may be able to provide insights into the complex problems of gerontology and geriatrics.

AIDAN BROWN, Dalhousie University
Peroxisome homeostasis

Peroxisomes are eukaryotic organelles that perform many metabolic functions, including fatty acid oxidation. Enzymes within peroxisomes are imported post-translationally and are guided through the import process by a cycling receptor; in mammals this protein is Pex5. The import process involves the ubiquitination of Pex5 on the peroxisome membrane. Maintenance of peroxisome numbers requires balance between proliferation and degradation. A receptor for degradation of peroxisomes uses ubiquitin to accumulate on peroxisomes – could the ubiquitin involved in protein import also play a role in peroxisome degradation? To address this question we have developed stochastic computational models of the Pex5 cycle at the peroxisome membrane and use them to track the ubiquitin involved in the Pex5 import cycle. Recently, a model of export-driven import

of cargo proteins was proposed, where Pex5 removal from the membrane is coupled to the translocation of the cargo across the membrane. We modeled conventional, uncoupled import and a newly proposed model of coupled export-driven import of cargo proteins. Both uncoupled and directly coupled import resulted in the peroxisomal Pex5 and ubiquitin both increasing as the amount of protein cargo increased, the opposite of the expected behaviour if the ubiquitin involved in import is also participating in degradation. However, with protein translocation cooperatively coupled to Pex5 export we find the opposite trend of decreasing ubiquitin levels with increasing protein cargo. This natural buildup of ubiquitin at low protein cargo levels suggests that ubiquitin could play a dual role in both peroxisome protein import and peroxisome degradation.

JOANNA MILLS FLEMMING, Dalhousie University
Challenges in Marine Statistical Ecology

Coastal nations like Canada have always depended on the ocean for their food security, economic activity and cultural well-being. Ocean activities today range from fishing, to tidal power, offshore oil and gas, sea bed mining, and marine pharmaceuticals. Human development of the ocean is poised to massively expand in the next few decades.

Statisticians are making meaningful contributions to advancing our understanding of the oceans. This information will be critical for the sustainable management of ocean resources, especially in the face of environmental shifts like global climate change. Herein we present three such projects, in each case providing details of the scientific question of interest, the statistical methodologies required and the results obtained.

The first project involves the estimation of critical population dynamics of young north Atlantic cod using multivariate state space models. The second presents a general formulation for mixed effects hurdle models that yields accurate estimates of abundance of critically endangered hammerhead sharks. Finally, the third project discusses new and exciting opportunities for the development of appropriate statistical methodologies for use within the Ocean Tracking Network (OTN), a global project that aims to establish a new and unique ocean observation system, centered on scientifically documenting marine animal movements, habitat use, and survival, in relation to changing chemical and biological ocean conditions.

ANDREW IRWIN, Mount Allison University
Statistical models of phytoplankton niches in a changing ocean

Anthropogenic changes in the Earth's climate system are expected to have dramatic consequences for the oceans, altering the flows in biogeochemical cycles and the dynamics of microscopic primary producers. We combine phytoplankton occurrence and abundance data with environmental variables to obtain ecological response functions for individual species. These response functions can be reduced to a simple description of phytoplankton realized niches. Differences in species niches suggest that it may be possible to incorporate the diversity of phytoplankton in predictions of changes over the next century.

ARNOLD MITNITSKI, Dalhousie University
System biology mechanics of aging: A stochastic dynamics model

The aging process can be represented as a process of accumulation of various health related deficits (broadly defined that include signs, symptoms, illnesses, functional limitations, laboratory abnormalities of the physiological indices, etc.) over the life course. Such data (essentially multidimensional) can be integrated into a single state variable representing the health status of the individual (a fitness/frailty index). The individual trajectories of the index are highly dynamic and show complex stochastic behavior. We present an empirical evidence of that the health trajectories of the index show the Markov property (quickly forgetting the past). Next we consider a stochastic model which allows accurately characterize the major age related patterns in deficit trajectories. This model is represented by the system of the Kolmogorov equations (either partial or different-differential) with the time dependent (i.e., age dependent) coefficients. We consider an important case when the variables can be divided by fast and slow representing two general processes: the fast process of damage/repair and the slow process of changes in the parameters representing repair (i.e. recovery) caused by the environmental damages. For the system of different-differential equations, the analytical solutions can be found under the assumption of quasi-stationarity. The statistical distributions of the quasi-stationary solutions closely resemble the patterns observed in the large-scale longitudinal databases

worldwide previously considered as empirical facts and now derived from a theoretical model. The latter sheds light to the general system biological mechanisms underlying complex process of aging.

FERNANDO PENA, Geriatrics Medicine Research unit, Dalhousie University
Trajectories of changes in health status over fourteen years of older adults using a multi-state modeling.

Changes in health show complex dynamics but can be summarized using a multi-state transition modeling approach. Our objective was to investigate, in people aged 70 years and older, whether changes in frailty status and mortality risk depend on baseline health, using a stochastic model of frailty state transitions. We performed secondary analysis of data from the Yale Precipitating Events Project, a cohort study based in New Haven CT, of non-disabled people aged $70+$ years ($n = 754$), assembled in 1998 and reassessed every 18 months. Thirty-six dichotomized variables (deficits) were used to calculate each individual's health status, combined in a frailty index. Transitions in the number of deficits over each time interval were represented by the Poisson law, with the Poisson mean dependent on the deficit numbers at baseline. Logistic regression was used to estimate mortality parameters over 162 months of follow-up. The model predicts a variety of changes in health status. Over 14 years of follow-up, the slope of the Poisson mean remained unchanged (0.77 ± 0.04) while the intercept (characterizing the transitions of those who had zero deficits at baseline) increases to 8.5. At the same time, the probability of death accelerated. People with zero deficits have a 20% chance of dying during the first 90 months, then slightly accelerates. The FI increased significantly more slowly in longer lived individuals (life-span $90+$) compared to the individuals whose life span was bellow age 90. The model is valuable for estimating how changes in health can influence mortality in older adults.

SWADHIN TANEJA, Dalhousie University
Fracture model of bacterial growth

The peptidoglycan (PG) cell wall is a key determinant of shape in "rod-shaped bacteria". However the mechanism guiding the growth of this elastic network of cross-linked PG (called sacculus) that maintains the integrity and shape of the rod-shaped cell remains a puzzle. We propose that the known anisotropic elasticity and anisotropic loading, due to the shape and turgor pressure, of the sacculus is sufficient to direct small gaps in the sacculus to elongate around the cell, and that subsequent repair leads to longitudinal growth without radial growth. We computationally show in our "Anisotropically stressed anisotropic elasticity model" small gaps can extend stably in the circumferential direction for the known elasticity of the sacculus. We suggest that patches of cytoskeletal protein, found recently, that propagate circumferentially in the cell wall are associated with these gaps and are steered with this common mechanism. We also show that small changes of elastic properties can in fact lead to bi-stable propagation of gaps, both longitudinal and circumferential, that can explain the bi-stability in patch movement observed in mutants.