# Modeling and Theory in Population Biology

Lead organizer:
Noah A Rosenberg (Stanford University)

Organizing committee:
Mark Broom (City, University of London),
Emilia Huerta-Sanchez (Brown University),
Sarah P Otto (University of British Columbia),
Ailene MacPherson (Simon Fraser University),
Maria Servedio (University of North Carolina),
John Wakeley (Harvard University)

May 19–24, 2024

## 1 Overview of the field

A five-day workshop was held May 19-24, 2024 at Banff International Research Station on Modeling and Theory in Population Biology. This workshop was the culmination of a five-month Hybrid Thematic Program, the first of its kind (`https://www.birs.ca/events/2024/5-day-workshops/24htp001`). In this document, we provide a report on the Hybrid Thematic Program, covering both the five-month online component and the five-day in-person workshop.

Phenomena such as the spread of alleles in populations, the coexistence of competing species in an ecological community, the branching patterns of species in evolutionary trees, and the dynamics of infectious diseases in emerging epidemics are linked by a shared mathematical tradition of population-biology modeling and theory. Problems concerned with the biology of populations span multiple biological subfields, including demography, ecology, epidemiology, evolution, population genetics, and phylogenetics. The mathematical study of such problems draws on techniques from diverse mathematical areas, including combinatorics, mathematical statistics, probability, and dynamical systems, and it is largely concerned with the construction and analysis of mathematical population models and the use of such models for data analysis.

The COVID-19 pandemic was arguably a high point in the demonstration of the scientific and societal value of mathematical and theoretical population biology. Diverse mathematical scientists from many subfields in the community of mathematical population biologists produced rapid research contributions of critical importance, established themselves as influential experts on the science of the pandemic, and provided epidemiological and evolutionary expertise to governments and the public.

The mathematical population biology community's collective ability to pivot and provide the needed expertise during the pandemic has illustrated, among ourselves and within the scientific community more generally, the mathematical unity of the seemingly diverse branches of mathematical population biology.

While mathematical studies in demography, ecology, epidemiology, evolution, population genetics, and phylogenetics each have their own distinctive features, the areas are linked by overlapping traditions and shared mathematical approaches: identification and analysis of equilibria, investigation of mechanistic dynamics, network-based methods and spatial modeling, modeling of stage transitions, biological optimality arguments, and the precise mathematical formulation and exploration of the consequences of verbal models, to name a few [33, 35]. During the pandemic, major contributions to mathematical epidemiology and evolution were made by researchers whose PhDs were focused on seemingly distant biological topics—such as evolutionary game theory, gene expression evolution, and spatial population genetics—all relying on a core of shared mathematics and shared principles of modeling in population biology.

This Hybrid Thematic Program sought to crystallize central ideas common across mathematical modeling and theory in population biology, and to promote mathematical studies at intersections among linked areas of demography, ecology, epidemiology, evolution, population genetics, and phylogenetics, considering connections both across their topics of investigation and in the techniques that they employ. As part of this effort, the program also sought to clarify central long-term challenges of mathematical population biology, including those revealed by the community's participation in the response to the COVID-19 pandemic.

## 2    Recent developments and the plan of the Hybrid Thematic Program

The Hybrid Thematic Program focused on "modeling" and "theory" in population biology. We consider population biology to include the various domains of biology that examine phenomena involving populations: principally demography, ecology, epidemiology, evolution, population genetics, and phylogenetics. The focus is on mathematical studies in the service of biological knowledge. "Modeling" is the process by which models are built to mathematize biological phenomena, and then investigated to discern conclusions about the biological systems that they describe. Examples include construction of disease transmission models in infectious disease epidemiology and population-genetic dynamical systems in evolutionary biology. "Theory" entails the mathematical development of broad areas of connection to biological systems, such as coalescent theory in population genetics and foraging theory in studies of ecology and animal behavior.

The main objectives of our Hybrid Thematic Program were to capitalize on the energy that has been produced among mathematical and theoretical population biologists in order to organize the community and enhance the science of the field. As a result of the field's contributions during the pandemic, the value of mathematical population biology can be seen more easily than ever before——by members of the field, by others in the scientific community, and by the public. Nevertheless, an organizational gap has existed in the community's activities. The research field focused on the mathematical biology of populations has had no organized community-based forum for such functions as identifying its research challenges, facilitating support for its junior researchers' development, and advocating for its value in the scientific community.

Some specific subfields of mathematical population biology have partial overlap with subject-area professional societies such as the American Society of Naturalists, Genetics Society of America, and Society for the Study of Evolution, as well as with the mathematically broad Society for Mathematical Biology and European Society for Mathematical and Theoretical Biology. In general, however, no existing professional organization has centered on this community of mathematical and theoretical researchers. Focused energy on the discipline and its community has largely relied on efforts of individual scientists and small groups, such as the committee of the biennial Mathematical Models in Ecology and Evolution meeting, rather than on an organized community effort.

We envisioned this Hybrid Thematic Program as a catalytic event for an ambitious plan to found an international professional society, the Society for Modeling and Theory in Population Biology. During the five months of the program, we conducted a series of activities to both advance the science of the field and cultivate its scientific community. In particular, we conducted several online series of events, targeted at promoting shared values that we seek to codify in the emerging professional society; some of these events focused explicitly on trainees.

1. **MINI-SYMPOSIA ON MODELING AND THEORY IN POPULATION BIOLOGY.** Online mini-symposia enable several researchers to comment on a shared modeling area or technique. We sought to conduct online mini-symposia about the role of the field in general as well as about focal research areas.

2. **MATHEMATICAL POPULATION BIOLOGY AND SOCIETY.** We planned an online seminar series in which leaders of the field could share their experiences working with policymakers and public outreach on societal challenges, covering both the scientific content of their expertise as well as the experience of their outreach interactions. This series connected COVID-related work with achievements in such areas as conservation biology and forensic genetics. Through this series, we aimed to celebrate the societally relevant work of our community members and to promote future activities in this area.

3. **EARLY-CAREER RESEARCH.** We organized a series of seminars by postdocs and advanced graduate students to provide a forum for emerging researchers at the forefront of the field.

4. **CAREER DEVELOPMENT.** We arranged events to focus on particular aspects of career development, on topics relating to the academic experience of modeling and theory researchers.

5. **MODELING AND THEORY COMMUNITY.** We arranged events focused on building interactions among trainees and senior researchers. We planned both online happy hours as well as structured discussions of communuity-related topics.

6. **REFLECTIONS ON THE HISTORY OF MODELING AND THEORY.** Interviews with members of the field contribute to understanding the scientific development of research areas and building a sense of history for its long tradition. We conducted recorded interviews with major figures in the field.

7. **SOFTWARE TUTORIALS.** We organized sessions in which the authors of major software packages taught software techniques to students and other researchers.

At the conclusion of the 5-month program, with the energy and enthusiasm developed over many months, we planned the 5-day in-person culmination of the program to focus on presentations of current research. We also arranged to include discussions of organizational aspects of the formation of the professional society.

# 3 Presentation highlights

## 3.1 Online events

**MINI-SYMPOSIA ON MODELING AND THEORY IN POPULATION BIOLOGY.** In the kickoff event for the Hybrid Thematic Program (January 11, 2024), **Maria Servedio** (University of North Carolina) presented an overview of the role of theoretical approaches as a method of testing verbal hypotheses in evolutionary biology. **Marcus Feldman** (Stanford University) covered highlights in modeling and theory over his long tenure as editor of the journal *Theoretical Population Biology*. **Joel Cohen** (Rockefeller University) described observations across science of *Taylor's law*, which relates the variance of the population density of individuals to the corresponding mean. Finally, **Tanja Stadler** (ETH Zürich) discussed population modeling during the COVID-19 pandemic, including her role as the leader of the COVID commission in Switzerland.

A second mini-symposium focused on *phylogenetic models*, which describe the divergence of evolutionary lineages in time (May 8, 2024). This mini-symposium was connected with an upcoming special issue of *Philosophical Transactions of the Royal Society B* on phylogenetic models, timed to commemorate the pioneering 1925 paper by G. Udny Yule [41]. **Simon Tavaré** (Columbia University) introduced the early history of the Yule birth process as a method in probability theory and stochastic processes. **Amaury Lambert** (Ecole Normale Supériure) provided observations about the ways in which Yule's paper has been cited, adding new historical observations. **Katia Koelle** (Emory University) discussed phylodynamics and the application of phylogenetic models to the study of phenomena in epidemics and infectious disease.

**MATHEMATICAL POPULATION BIOLOGY AND SOCIETY.** Talks in this series connected modeling research to societal applications. **Bruce Weir** (University of Washington) discussed the use of population genetics in contributing to the use of DNA evidence in forensic science, drawing from long experience working with forensic cases and guidelines (January 17, 2024). **Marissa Baskett** (University of California, Davis) described models of distinct ecological states in kelp forests and sea urchin populations over space and time, explaining how the models were able to assist in coastal management of a near-shore Pacific ecosystem after an ecological disturbance (April 16, 2024).

**EARLY-CAREER RESEARCH.** Talks by trainees provided PhD and postdoctoral researchers with a forum to present to a global online community. The first session focused on phylogenetic and population-genetic models (February 28, 2024). **Francois Bienvenu** (ETH Zürich) discussed branching and merging of lineages in the modeling of phylogenetic trees and networks. **Mia Miyagi** (Brown University) examined introgression and incomplete lineage sorting in the context of population divergence on a recent phylogenetic time scale, also discussing topics on the analysis of gender in human-genetic studies.

In a second event (April 3, 2024), **Lenore Pipes** (University of California, Berkeley) explained algorithms for phylogenetic assignment of DNA from large-scale environmental sequencing. **Maria Martignoni** (Hebrew University of Jerusalem) studied the role of microbes in facilitating biological invasions. Finally, in a third event (May 1, 2024), **Maria Kleshnina** (Queensland University of Technology) described the evolution of cooperation in scenarios with heterogeneous actors. **Alex Stein** (Queen Mary University of London) examined evolution in cancer, covering birth–death processes and the frequency spectrum of mutations.

**CAREER DEVELOPMENT.** Career development sessions focused on challenges for theoreticians in obtaining and serving in different types of faculty positions, recognizing that theoretical population biology research has a dual need of addressing biological research goals while using and producing sufficiently interesting mathematical approaches. The first panel (January 30, 2024) covered challenges of biological research in departments of mathematics, statistics, and physics, and featured panelists **Ben Ashby** (Simon Fraser University), **Caroline Colijn** (Simon Fraser University), **Laura Kubatko** (Ohio State University), and **Daniel Weissman** (Emory University). The second panel (March 26, 2024) focused on biology departments and featured **Claus Rüffler** (Uppsala University), **Maria Servedio** (University of North Carolina) and **Jeremy Van Cleve** (University of Kentucky).

**MODELING AND THEORY COMMUNITY.** Participants in the Hybrid Thematic Program expressed considerable interest in the teaching of mathematical population biology. A panel of experts (March 20, 2024) including **Troy Day** (Queen's University), **Anna Dornhous** and **Joanna Masel** (University of Arizona), and **Pleuni Pennings** (San Francisco State University) discussed pedagogical strategies for engaging a variety of students from applied math, biology, and computer science in the methods and topics of mathematical population biology. In another event focused on enhancing the community of modeling and theory researchers, **Alex Diaz-Papkovich** described the importance of Wikipedia as a tool for public learning about population genetics, tracing the manner in which research articles in human population genetics are cited in Wikipedia entries (April 9, 2024).

**REFLECTIONS ON THE HISTORY OF MODELING AND THEORY.** Interviews have covered the careers of important scientists in the field. **Montgomery Slatkin** (University of California, Berkeley) discussed his career beginning as an applied mathematician and transitioning into mathematical research in population biology (February 20, 2024). **Deborah Charlesworth** (University of Edinburgh) discussed her work as an evolutionary biologist with a theoretical perspective (April 24, 2024). A final interview with evolutionary biologist **Brian Charlesworth** (University of Edinburgh) completed the series (May 14, 2024).

**SOFTWARE TUTORIALS.** A major area by which modeling and theory researchers connect with communities of empirical biologists is through modeling and theory software. **Jerome Kelleher** (University of Oxford) gave a tutorial on the use of `msprime` for backward simulation of population-genetic lineages (February 13, 2024). **Ben Haller** (Cornell University) gave a tutorial on the use of `SLiM` for forward simulation in population genetics (March 13, 2024).

## 3.2 In-person workshop

The in-person workshop occurred at the conclusion of the Hybrid Thematic Program. Many of the scientific talks at the in-person workshop covered general aspects of modeling and theory, including challenges and opportunities for the overall scientific field. Talks were also focused on specific domains for application of models and development of theory.

**SPATIAL MODELS.** Ecological and evolutionary processes take place in a spatial environment, and population models often make use of a geometry of interactions among individuals and populations. **Ailene**

**MacPherson** (Simon Fraser University) discussed methods of inferring local adaptation in models that consider migration, selection, and "spice," the extra elements of the model that are typically of interest. A Bayesian inference framework involves a core conceptual structure that contains *processes* encoded by models, *patterns* in data, and *context* that supplies prior distributions on parameters. The term "spice" for the extra features that extend beyond basic assumptions became a running metaphor invoked throughout the workshop.

**Daniel Weissman** (Emory University) discussed the concept of *hitchhiking*, in which genomic neighbors of a favorable genetic variant increase in frequency along with the favorable variant. The spatial distance along the genome is related to the strength of selection on the favorable variant and the time that it takes for the variant to reach a high frequency. **Oana Carja** (Carnegie Mellon University) examined evolutionary dynamics with concepts of discrete graphical structures, arguing that network representations can be used to understand fixation probabilities beyond standard lattice or deme models [22]. Classic concepts of network theory, such as the mean node degree, variance of node degree, and counts of connected triangles influence the resulting theory; they can be used together with classic population-genetic ideas such as the Moran model of birth and death in populations in order to study spatial patterns in stem cells in bone marrow [23].

**POPULATION MODELS: GENERAL PRINCIPLES.** Overarching principles of population modeling influence many applications. **Mark Broom** (City, University of London) clarified scenarios in which distinct ways of taking averages can lead to fallacies in the reasoning used by models, noting in particular a distinction between an average of ratios and a ratio of averages in optimal foraging theory. **Brandon Ogbunu** (Yale University) spoke about major directions for theory in the area of mathematical epidemiology of infectious diseases, reflecting on the context-dependence of mutations in viruses and the way in which evolutionary theory of the trajectory of virulence can be important in policy guidance in epidemics. A notable concept in understanding mutational impact is epistasis, "the surprise at the phenotype when mutations are combined."

**Caroline Colijn** (Simon Fraser University) covered multiple uses of models, such as for quantitative exploration about a scenario, for proof of a concept, or for prediction about data. A distinction exists between modeling studies that answer a biologically relevant question—a central theme of the workshop—and modeling studies that focus on mathematical properties and are not performed in the service of the biology [32]. **Hamish Spencer** (University of Otago) emphasized the historical dynamics that underlie ecological and evolutionary systems, discussing examples from evolutionary biology pioneers Theodosius Dobzhansky and Richard Lewontin on explaining the existence of genetic variation. For example, it is unlikely that a set of random fitness values maintains all $n$ alleles in a population, but it is not unlikely that a polymorphism with $n$ alleles can evolve in a mutation model [36]. A similar ease of maintenance of polymorphism is observed in a model that contains a deteriorating environment [37]. Modeling in ecology and evolution often emphasizes equilibrium analyses, which discard the history, and the importance of contingency and context advocate for the understanding of dynamical processes rather than merely optimality and equilibria.

**GENEALOGICAL MODELS.** Mathematical models of genealogies are central in population genetics, understanding evolution by proceeding backward from the present to explain the ancestry of sampled data. **Marcy Uyenoyama** (Duke University) discussed two concepts examined in genealogical models, namely the $F_{ST}$ measure of identity in a population, and linkage disequilibrium (LD), or association in the appearance of alleles at different loci. Many formulations of $F_{ST}$ have been proposed, as descriptive summaries, for statistical inference, or as population parameters [38]. A concept linking $F_{ST}$ measures with LD is *identity disequilibrium*, which measures association in the appearance of homozygous genotypes across loci [28].

**Emilia Huerta-Sanchez** (Brown University) discussed the use of models and statistics in the inference of human population history, particularly for the detection of ancient introgression in modern humans. Models seek to infer genomic segments in modern humans that trace to extinct groups such as Neanderthals. **Matthew Osmond** (University of Toronto) presented new progress in the study of a classic structure, the *ancestral recombination graph*, describing its application in the inference of the spatial ancestry of a population [14].

**COMPETITION, COOPERATION, AND CONFLICT.** Ecology and evolutionary biology have long examined problems involving individual interactions. Such interactions can have a variety of types of behaviors, including cooperation, competition, and conflict. **Jeremy Van Cleve** (University of Kentucky) studied $n$-player games that generate tipping points, where systems switch between stable attractors with small changes in parameters. Methods such as *sparse identification of nonlinear dynamics* (SINDy) [8] and "equation discovery" [5] may be useful in identifying dynamical equations consistent with observed social behavior.

**Sasha Dall** (University of Exeter) described asocial learning in the context of social interactions, involving competition between two strategies: "producers" and "scroungers." Producers invest in finding a food source, whereas scroungers exploit the food source found by others. Negative frequency dependence influences behavioral dynamics in a producer–scrounger setting, as each strategy is promoted by the existence of the other. **Egor Lappo** (Stanford University) treated the competitive game of chess as a model of cultural transmission. Factors such as conformity bias, frequency-dependent bias, and prestige bias can influence the moves that players make at the end of the opening in a chess game. In a large database of games, the frequency with which certain moves are made is seen to be the result of the various different cultural transmission biases. The approach adapts a Wright-Fisher model from population genetics to cultural data [24].

Continuing a theme of reevaluating fundamental concepts, **Joanna Masel** (University of Arizona) argued that in the short term, vital rates may be more relevant concepts than the concept of *fitness* for understanding population dynamics. Different aspects of the biological success of a lineage can be investigated, including the probability of its establishment and its growth when it is rare. **Daniel Smith** (University of Arizona) described different types of competition, including exploitative competition, in which individuals compete for a shared resource, and interference competition, in which one organism directly restricts access of another organism to a resource. Evolutionary game theory models of competition assist in clarifying the circumstances in which coexistence occurs in a competitive situation.

**Ben Allen** (Emmanuel College) considered mathematical formalism in social evolution, seeking to clarify the meaning of concepts of relatedness and inclusive fitness in one of the more challenging theoretical settings for evolutionary biology. A key distinction in social interaction models is between actor-centered and recipient-centered perspectives on an interaction.

**PHYLOGENIES, TREES, AND MACROEVOLUTION.** Evolutionary trees produce a rich source of challenges and opportunities at the intersection of mathematics and biology. **Julia Palacios** commented on distance metrics that can be defined on various different tree spaces, including the set of labeled trees with $n$ leaves and the corresponding set of unlabeled trees. An innovation is to focus on distances between ranked tree shapes, a class of trees that is more numerous than the unlabeled trees and less numerous than the labeled trees. The Frechet mean provides a key concept, specifying a center of a discrete tree space [34].

**Noah Rosenberg** (Stanford University) described the enumerative combinatorics of evolutionary trees, with a focus on the concept of *labeled histories*. For a leaf-labeled tree topology, a labeled history specifies a sequence in which its divergences take place. The classic concept of labeled histories can be generalized to allow for simultaneous bifurcations [19] and for non-simultaneous and simultaneous multifurcations. The enumerations have analogous interpretations in evolutionary biology and in the sequences by which the games of single-elimination sports tournaments can be played. **Chloe Shiff** (Stanford University), continued the discussion of combinatorial enumeration of evolutionary trees, focusing on *perfect phylogenies*, a type of unlabeled tree in which each leaf is associated with a discrete sample size. Enumerative combinatorics of perfect phylogenies can proceed through derivation and asymptotic analysis of a generating function, generalizing past results on unlabeled trees.

**Lindi Wahl** (University of Western Ontario) investigated bacterial extinction, a feature of long-term bacterial evolution that requires explanation [25]. A differential equation predator–prey system with bacteria as the prey and phage as the predator enables a model that predicts dependencies of the extinction probabilities. **Carolin Kosiol** (University of St. Andrews) investigated gene trees, population trees, and species trees, considering a variety of statistical principles and algorithms. A new approach seeks to incorporate long-term balancing selection at the interface of population-genetic and phylogenetic inference [7].

**Benjamin Peter** (University of Rochester) continued the statistical thread of the session, discussing principal components analysis (PCA) in population genetics. PCA has many counterintuitive behaviors, including a sampling dependence that can influence the direction of the first principal component [13]. Simple summary statistics of genetic variation can be related through a geometrical perspective to features of principal components analysis [30]. New work demonstrates that contrary to frequent claims, certain patterns in the $F_3$ statistic for analysis of three populations need not reflect a history of population admixture.

**SELECTION AND ADAPTATION.** Mathematical evolutionary models seek to explain the mechanistic action of natural selection and its role in explaining adaptation of organisms to their modes of life. **Troy Day** (Queen's University) discussed the relationships of genotypes to fitness through the *distribution of fit-*

*ness effects* and a classic approach, *Fisher's geometric model*. Random fitness maps provide a basis for understanding the distribution of fitness effects; they can be enumerated and analyzed in different settings, including in relation to a "fit" ancestor. **Yoav Ram** (Tel Aviv University) examined the potential role of the phenomenon of aneuploidy, in which an organism has an abnormal number of chromosomes, during selection leading to adaptation. Aspects of the mutation process influence whether aneuploidy can be regarded as a step leading to adaptation or simply a diversion [20].

In a remote talk, **Andy Clark** (Cornell University) discussed the widespread abundance of transposable elements, sections of DNA that move from one place in a genome to another [39]. The mathematical effort to explain their abundance traces to models in the 1980s [10]. Small RNA sections known as piRNAs interfere with the RNA produced by transposable elements, generating an evolutionary arms race involving both transposable elements and piRNAs, with much potential for evolutionary modeling [26].

**Carl Bergstrom** (University of Washington) introduced a framework for understanding natural selection in relation to information theory. The concept of "loss" can be understood as the cost of a mismatch between a biological strategy and its environment. The "regret" is the cost of needing to learn the optimal strategy, "regretting" that it is not immediately known. In a model of potential mechanisms leading to a match of strategies and environments, the process of natural selection is not far from an optimum in minimizing regret. Continuing a theme of understanding evolution with frameworks common in computational science, **Dan Weinreich** (Brown University) described the population genetics of phenotypic noise, explained as fluctuations in an organismal property over time. The dynamical approach of *modifier theory* in population genetics can treat phenotypic noise like a mutation modifier [9]. It is convenient to distinguish modifiers that act during reproduction and those that act during development.

**THE ECOLOGY/EVOLUTION INTERFACE.** Evolutionary models often arise from ecological considerations, and tools for analyzing ecological data or evolutionary data can benefit from parallel problems in the other area. **Gili Greenbaum** (Hebrew University of Jerusalem) investigated mathematical models of gene drives, a scenario in which an organismal variant of particular genetic background is introduced to a population with the aim of reducing the population size of a competing variant, typically in pest species. Because field trials cannot be performed, mathematical models have a particular role in predicting the risks and likely outcomes of gene drives, and the combination of ecological and evolutionary ideas is essential [18]. An outgrowth of the effort is an attempt to encode diverse models across the field of population biology in an executable archive in order to facilitate their wider use. **Maike Morrison** (Stanford University) described the use of statistics borrowed from population genetics, namely the $F_{ST}$ measure of allele-frequency differences across populations, for the problem of evaluating *compositional variability* in ecological data on microbiomes. In an experimental system involving an antibiotic perturbation to human gut microbiomes assessed via stool samples, the $F_{ST}$-based "FAVA" measures the temporal variation in microbiome composition, accounting for unevenness in the times of sampling.

**Viggo Andreasen** (Roskilde University) described models of infectious diseases [1] and how they were adapted during the COVID-19 pandemic, with particular reference to Denmark. The spread of early variants (e.g., Alpha) was well described by classic selection models, but later variants (Delta, Omicron) required simultaneously accounting for evolution and vaccination. Variant spread was best described by changes in Malthusian fitness (exponential growth rates), in contrast to Wrightian fitness (number of offspring), which is more relevant when determining how seasonal, behavioral, or public health changes affect spread [40].

Mathematical ecological and evolutionary models often seek to explain the existence or maintenance of an observed phenomenon. **Rohan Mehta** (Elmhurst University) modeled the phenomenon of *autotomy*, in which individuals lose a body part that provides food to a predator. The question is whether autotomy would deter predators who are satiated by the lost body part, or attract predators to eat the prey organism. Autotomy is widely distributed taxonomically, but rare [16]. The model, which showcases a strategy of encoding verbal hypotheses with mathematics, finds that a zone of parameter space exists in which a prey species maintains an autotomy strategy [27]. In another talk at the ecology–evolution interface, **Bryn Wiley** (University of British Columbia) discussed when hybridization can speed up adaptation to a changed environment, despite the reduction in hybrid fitness caused by genetic incompatibilities [21].

**MODES OF REPRODUCTION.** The mathematical structure of reproduction, in which genotypes are transmitted from parent to offspring according to stochastic mechanisms, underlies many evolutionary models.

**Mark Tanaka** (University of New South Wales) asked why facultative parthenogenesis, a mode of reproduction in which individuals have the capability of reproducing sexually or asexually, is not more common. The problem can be understood in terms of condition-dependent evolution of sex [17]. In a model with X-linked recessive alleles that allow females to reproduce parthenogenetically—with XX and XU genotypes giving rise to sexual females, and UU producing parthenogenetic females—facultative parthenogenesis can evolve in a sexual organism in a setting with low dispersal. **Sally Otto** (University of British Columbia) described work to generalize classic diploid models of selection and drift to life cycles that undergo an alternation of generations between haploidy and diploidy (as seen in many fungi, algae, and other protists). While appearing similar to two-sex models with sex chromosomes or *arrhenotoky* (haploid males and diploid females), the stochastic properties with alternating generations are different, as are the conditions maintaining variation [4].

**DEMOGRAPHY AND STAGE STRUCTURE.** By taking into account that biological phenomena such as reproductive behavior vary across life stages, mathematical models can examine population dynamics in stage-structured populations. Building on age-structured models with complex phenotypes [11], **Amy Forsythe** (University of British Columbia) considered individual heterogeneity in vital rates within age classes. In Markov models, phenotypic heterogeneity can be collapsed, without losing information about population dynamics (including transient behavior), as long as parental phenotypes do not influence offspring phenotype. Stage structure extends beyond demographic effects, influencing the evolutionary process [3], as examined by **Maria Orive** (University of Kansas). Classic models of quantitative genetics assume sexual reproduction and find that the response to selection depends on the additive genetic variance, but the response to selection with stage structure and clonal reproduction depends also on the total heritable variance [29].

**Ulrich Steiner** (Free University of Berlin) continued the study of stage structure with an investigation of bacterial aging. In binary fission in bacteria, daughter cells can inherit phenotypes asymmetrically. Stress response can be measured with gene expression, and single-cell data enables detailed understanding of demographic fates in the daughter cells. The integral projection matrix approach of mathematical demography [15] can take into account a Markov transition that represents an increase in cell size.

**CULTURAL AND SOCIAL EVOLUTION.** Cultural evolution models consider the transmission and dynamics of cultural behaviors in populations over time. **Oren Kolodny** (Hebrew University of Jerusalem) discussed the benefits of the agent-based modeling tradition for several problems in cultural evolution. While agent-based simulation models have typically been considered as a method for tracking large numbers of factors, another use is to treat them similarly to other modeling strategies, for example, as a logical device to formalize verbal arguments and to explore parameters in isolation. **Kaleda Denton** (Stanford University) developed mathematical models of the cultural dynamics of conformity. A conformist adopts a cultural variant at a rate greater than its frequency in the population; an anti-conformist adopts it at a rate less than its frequency. An early cultural evolution model of conformity [6] considered a scenario in which an actor observes 3 other individuals and adopts a behavior based on its frequency among the 3; new models can now proceed in the case that the actor observes $n$ individuals, where $n \geq 3$ is arbitrary. Chaotic dynamics can develop under certain configurations with $n$ as small as 5.

**Nicole Creanza** (Vanderbilt University) discussed the tool repertoire size of populations, noting that the repertoire size sometimes decreases in small isolated populations. The repertoire size can also be related to other factors, such as modes of learning, levels of environmental fluctuation, and levels of specialization in the population. Interestingly, cultural patterns seen in humans are paralleled by patterns in birds, with, for example, larger birdsong repertoires seen in larger connected populations [12].

**WORKING GROUPS.** In addition to the scientific program, the participants conducted discussions about the future of the Society for Modeling and Theory in Population Biology. The working groups discussed plans for future community-building, in-person conferences, publications, and teaching activities. The event concluded with plans for organizational efforts and future activities in all of these areas.

# 4 Progress from the Hybrid Thematic Program

## 4.1 Scientific progress

The scientific sessions of the in-person workshop advanced progress in the areas of spatial models; genealogical models; competition, cooperation, and conflict; phylogenies, trees, and macroevolution; selection and adaptation; the ecology/evolution interface; modes of reproduction; demography and stage structure; and cultural and social evolution. These topics built upon instances of many of the same areas that were discussed in the online sessions in advance of the workshop.

A highlight of the scientific progress throughout the entire Hybrid Thematic Program concerned general principles for population models, and efforts to characterize high-quality work in the field. A number of themes emerged across the talks.

- Mathematical models serve to promote biological understanding.
  **Oren Kolodny** and **Caroline Colijn** emphasized that modeling in population biology is a way of thought that serves the quest for biological knowledge. Mathematical models possess both a biological interest and a mathematical interest, and the researcher pursues the mathematical problems with a view toward solving the problem in population biology.

- Mathematical population biology has a long tradition.
  **Marcus Feldman**, **Amaury Lambert**, and **Marcy Uyenoyama** emphasized rich traditions in the area of modeling and theory, with some of the earliest ideas tracing back hundreds of years [2].

- Mathematical models formalize verbal arguments.
  **Maria Servedio**, **Rohan Mehta**, and **Mark Tanaka** showed examples of a classic role of population modeling—formalizing verbal models using mathematics, and using the mathematics to understand how the biological systems work.

- Updates in mathematics and computation extend classic theoretical ideas.
  **Matthew Osmond**, **Benjamin Peter**, and **Troy Day** found new ways to deepen long-extant modeling ideas such as the ancestral recombination graph, principal components analysis of genetic data, and the distribution of fitness effects for use with modern data sets and applications.

- Population biology is an ideal setting for applying advances in mathematics.
  **Oana Carja**, **Jeremy Van Cleve**, and **Chloe Shiff** illustrated the potential of modeling in population biology to benefit from quite recent developments in associated areas of mathematics, such as network theory, numerical analysis, and analytic combinatorics.

- Mathematical population biology advances mathematics.
  **Simon Tavaré**, **Julia Palacios**, and **Noah Rosenberg** illustrated that new mathematics can be developed in the search for biological knowledge, producing advances both in an area of evolution or ecology and in a mathematical area such as stochastic processes or combinatorics.

- Mathematical population biology builds broad connections across fields.
  **Carl Bergstrom** and **Nicole Creanza** demonstrated that population modeling makes intellectual connections well beyond evolutionary biology and ecology, to areas such as information theory and the human behavioral sciences.

- Core principles in mathematical population biology are continuously being queried.
  **Mark Broom**, **Hamish Spencer**, and **Joanna Masel** discussed principles that affect many aspects of the science of population modeling, providing perspectives on advancing the field in a general way beyond specific applications.

- Mathematical popiulation biology has great utility for empirical scientists.
  **Jerome Kelleher**, **Ben Haller**, **Lenore Pipes**, and **Gili Greenbaum** illustrated that software based on perspectives from population modeling has great potential to engage empirical researchers from across ecology and evolutionary biology.

- Mathematical population biology is consequential for real-world problems.
  **Tanja Stadler**, **Bruce Weir**, **Marissa Baskett**, **Brandon Ogbunu**, and **Viggo Andreasen** emphasized that modeling in population biology is hugely consequential, with potential to influence major areas of human activity such as forensic genetics, ecological restoration, and pandemic response.

The meeting characterized a number of challenges for future research. For example, **Oana Carja**, **Daniel Weissman**, **Yoav Ram**, **Gili Greenbaum**, **Maike Morrison**, and **Ulrich Steiner** suggested the potential of population modeling approaches to advance progress in relatively new areas of application, such as cellular development, cancer modeling, gene drives, microbiomes, and single-cell data. **Matthew Osmond** and **Ben Allen** discussed potential for new directions in the theory itself, in regard to genealogical models and social evolution models. **Brandon Ogbunu** and **Caroline Colijn** emphasized the importance of modelers' responsibility to be attentive to human dimensions of model predictions in an applied setting.

## 4.2  Community-building

This Hybrid Thematic Program was meant to spearhead an effort to develop a new professional society, the Society for Modeling and Theory in Population Biology, SMTPB. The effort to produce the proposal for the program generated 316 endorsements for the application and the idea of forming the society. By the conclusion of the Hybrid Thematic Program, we had accumulated a mailing list of more than 650 people.

Attendance data for the Hybrid Thematic Program were captured by the BIRS online platform. Excluding the three interviews, which entailed posted videos and did not include a real-time event component, the numbers of online attendees at the various events were:

- **Maria Servedio**, **Marc Feldman**, **Joel Cohen**, **Tanja Stadler**, kickoff event (January 11, 2024): 310.

- **Bruce Weir**, forensic genetics (January 17, 2024): 74.

- Career panel—mathematics, statistics, and physics departments (January 30, 2024): 75.

- **Jerome Kelleher**, `msprime` software (February 13, 2024): 126.

- Early-career speakers I (February 28, 2024): 64.

- **Ben Haller**, `SLiM` software (March 13, 2024): 64.

- Pedagogical strategies (March 20, 2024): 29.

- Career panel—biology departments (March 26, 2024): 33.

- Early-career speakers II (April 3, 2024): 26.

- **Alex Diaz-Papkovich**, Wikipedia (April 9, 2024): 38.

- **Marissa Baskett**, kelp forest ecology (April 16, 2024): 36.

- Early-career speakers III (May 1, 2024): 24.

- **Simon Tavaré**, **Amaury Lambert**, **Katia Koelle**, phylogenetic models (May 8, 2024): 87.

In addition, the in-person meeting (May 20-24, 2024) had 44 online attendees (25, 25, 17, 12, and 9 on the five days of the meeting). The number of people who attended at least one online event was 573.

After the Hybrid Thematic Program was approved, and during the preparation for the program, SMTPB was formed as a professional society, and more than 100 people have joined as members. At the conclusion of the Hybrid Thematic Program, we have an organizational structure and plans for the next activities, including further community-building and educational efforts. The program has made significant progress in celebrating the field, providing encouragement to community members, advancing scientific progress, and facilitating an organizational structure for future activities.

# Acknowledgments

# References

[1] V. Andreasen, F. B. Christiansen. Disease-induced natural selection in a diploid host. *Theoretical Population Biology* **44** (1993), 261-298. https://doi.org/10.1006/tpbi.1993.1029.

[2] N. Bacaër. *A short history of mathematical population dynamics*. Springer, London (2011).

[3] M. Barfield, R. D. Holt, R. Gomulkiewicz. Evolution in stage-structured populations. *American Naturalist* **177** (2011), 397-409. https://doi.org/10.1086/658903.

[4] K. Bessho, S. P. Otto. Fixation and effective size in a haploid–diploid population with asexual reproduction. *Theoretical Population Biology* **143** (2022), 30-45. https://doi.org/10.1016/j.tpb.2021.11.002.

[5] W. Bonaffé, T. Coulson. Fast fitting of neural ordinary differential equations by Bayesian neural gradient matching to infer ecological interactions from time-series data. *Methods in Ecology and Evolution* **14** (2023), 1543-1563. https://doi.org/10.1111/2041-210X.14121.

[6] R. Boyd, P. J. Richerson. *Culture and the evolutionary process*. University of Chicago Press, Chicago (1985).

[7] S. Braichenko, R. Borges, C. Kosiol. Polymorphism-aware models in RevBayes: species trees, disentangling balancing selection and CG-biased gene conversion. *bioRxiv* (2024). https://doi.org/10.1101/2023.12.11.571102.

[8] S. L. Brunton, J. L. Proctor, J. N. Kutz. Discovering governing equations from data by sparse identification of nonlinear dynamical systems. *Proceedings of the National Academy of Sciences USA* **113** (2016) 3932-3937. https://doi.org/10.1073/pnas.1517384113.

[9] O. Carja, J. B. Plotkin. The evolutionary advantage of heritable phenotypic heterogeneity. *Scientific Reports* **11** (2017) 5090. https://doi.org/10.1038/s41598-017-05214-2.

[10] B. Charlesworth, C. H. Langley. The evolution of self-regulated transposition of transposable elements. *Genetics* **112** (1986), 359-383. https://doi.org/10.1093/genetics/112.2.359.

[11] C. F. D. Coste, F. Austerlitz, S. Pavard. Trait level analysis of multitrait population projection matrices. *Theoretical Population Biology* **116** (2017), 47-58. https://doi.org/10.1016/j.tpb.2017.07.002.

[12] R. Crates, N. Langmore, L. Ranjard, D. Stojanovic, L. Rayner, D. Ingwersen, R. Heinsohn. Loss of vocal culture and fitness costs in a critically endangered songbird. *Proceedings of the Royal Society B* **288** (2021) 20210225. https://doi.org/10.1098/rspb.2021.0225.

[13] M. DeGiorgio, N. A. Rosenberg. Geographic sampling scheme as a determinant of the major axis of genetic variation in principal components analysis. *Molecular Biology and Evolution* **30** (2013), 480-488. https://doi.org/10.1093/molbev/mss233.

[14] P. Deraje, J. Kitchens, G. Coop. Inferring the geographic history of recombinant lineages using the full ancestral recombination graph. *bioRxiv* (2024). https://doi.org/10.1101/2024.04.10.588900.

[15] S. P. Ellner, M. Rees. Integral projection models for species with complex demography. *American Naturalist* **167** (2006), 410-428. https://doi.org/10.1086/499438.

[16] Z. Emberts, I. Escalante, P. W. Bateman. The ecology and evolution of autotomy. *Biological Reviews* **94** (2019), 1881-1896. https://doi.org/10.1111/brv.12539.

[17] L. Hadany, S. P. Otto. The evolution of condition-dependent sex in the face of high costs. *Genetics* **176** 2007, 1713-1727. https://doi.org/10.1534/genetics.107.074203.

[18] K. D. Harris. G. Greenbaum. Rescue by gene swamping as a gene drive deployment strategy. *Cell Reports* **42** (2023), 113499. https://doi.org/10.1016/j.celrep.2023.113499.

[19] M. C. King, N. A. Rosenberg. A mathematical connection between single-elimination sports tournaments and evolutionary trees. *Mathematics Magazine* **96** (2023), 484-497. https://doi.org/10.1080/0025570X.2023.2266389.

[20] I. Kohanovski, M. Pontz, P. V. Zande, A. Selmicki, O. Dahan. Y. Pilpel, A. H. Yona, Y. Ram. Aneuploidy can be an evolutionary diversion on the path to adaptation. *Molecular Biology and Evolution* **41** (2024), msae052. https://doi.org/10.1093/molbev/msae052.

[21] J. Kulmuni, B. Wiley, S. P. Otto. On the fast track: hybrids adapt more rapidly than parental populations in a novel environment. *Evolution Letters* **8** (2024), 128–136. https://doi.org/10.1093/evlett/qrad002.

[22] Y. P. Kuo, O. Carja. Evolutionary graph theory beyond pairwise interactions: Higher-order network motifs shape times to fixation in structured populations. *PLoS Computational Biology* **20** (2024), e1011905. https://doi.org/10.1371/journal.pcbi.1011905.

[23] Y. P. Kuo, C. Nombela-Arrieta, O. Carja. A theory of evolutionary dynamics on any complex population structure reveals stem cell niche architecture as a spatial suppressor of selection. *Nature Communications* **15** (2024), 4666. https://doi.org/10.1038/s41467-024-48617-2.

[24] E. Lappo, N. A. Rosenberg, M. W. Feldman. Cultural transmission of move choice in chess. *Proceedings of the Royal Society B* **290** (2023), 37964528. https://doi.org/10.1098/rspb.2023.1634.

[25] S. Louca, P. M. Shih, M. W. Pennell, W. W. Fischer, L. W. Parfrey, M. Doebeli. Bacterial diversification through geological time. *Nature Ecology and Evolution* **2** (2018), 1458-1467. https://doi.org/10.1038/s41559-018-0625-0.

[26] S. Luo, H. Zhang, Y. Duan, X. Yao, A. G. Clark, J. Lu. The evolutionary arms race between transposable elements and piRNAs in *Drosophila melanogaster*. *BMC Evolutionary Biology* **20** (2020), 14. https://doi.org/10.1186/s12862-020-1580-3.

[27] R. S. Mehta, J. A. Kraus. Eco-evolutionary dynamics of autotomy. *Theoretical Ecology* **14** (2021), 445-464. https://doi.org/10.1007/s12080-021-00507-9

[28] T. Ohta. Linkage disequilibrium between amino acid sites in immunoglobulin genes and other multigene families. *Genetical Research* **36** (1980), 181-197. https://doi.org/10.1017/S0016672300019790.

[29] M. E. Orive, M. Barfield, C. Fernandez, R. D. Holt. Effects of clonal reproduction on evolutionary lag and evolutionary rescue. *American Naturalist* **190** (2017), 469-490. https://doi.org/10.1086/693006.

[30] G. Oteo-Garcia and J.-A. Oteo. A geometrical framework for $f$-statistics. *Bulletin of Mathematical Biology* **83** (2021), 14. https://doi.org/10.1007/s11538-020-00850-8.

[31] J. Peña, L. Lehmann, G. Nöldeke. Gains from switching and evolutionary stability in multi-player matrix games. *Journal of Theoretical Biology* **346** (2014), 23-33. https://doi.org/10.1016/j.jtbi.2013.12.016.

[32] N. A. Rosenberg. Theory in biology, or biologically inspired mathematics? *Theoretical Population Biology* **102** (2015), 1-2. https://doi.org/10.1016/j.tpb.2015.01.002.

[33] N. A. Rosenberg. Fifty years of theoretical population biology. *Theoretical Population Biology* **133** (2020), 1-12.https://doi.org/10.1016/j.tpb.2020.04.001.

[34] R. Samyak, J. A. Palacios. Statistical summaries of unlabelled evolutionary trees. *Biometrika* 111 (2024), 171-193. https://doi.org/10.1093/biomet/asad025.

[35] M. R. Servedio, Y. Brandvain S. Dhole, C. L. Fitzpatrick, E. E. Goldberg, C. A. Stern, J. Van Cleve, J. Yeh. Not just a theory—the utility of mathematical models in evolutionary biology. *PLoS Biology* **12** (2014), e1002017. https://doi.org/10.1371/journal.pbio.1002017.

[36] H. G. Spencer, R. W. Marks. The maintenance of single-locus polymorphism. I. Numerical studies of a viability selection model. *Genetics* **120** (1988), 605–613. https://doi.org/10.1093/genetics/120.2.605.

[37] H. G. Spencer, C. B. Walter. Polymorphism and the Red Queen: the selective maintenance of allelic variation in a deteriorating environment. *G3 Genes Genomes Genetics* **14** (2024), jkae107. https://doi.org/10.1093/g3journal/jkae107.

[38] M. K. Uyenoyama. Wright's hierarchical $F$-statistics. *Molecular Biology and Evolution* **41** (2024), msae083. https://doi.org/10.1093/molbev/msae083.

[39] J. N. Wells, C. Feschotte. A field guide to eukaryotic transposable elements. *Annual Review of Genetics* **54** (2020), 539-561. https://doi.org/10.1146/annurev-genet-040620-022145.

[40] B. Wu, C. S. Gokhale, M. van Veelen, L. Wang, A. Traulsen. Interpretations arising from Wrightian and Malthusian fitness under strong frequency dependent selection. *Ecology and Evolution* **3** (2013), 1276-1280. https://doi.org/10.1002/ece3.500.

[41] G. U. Yule. II.—A mathematical theory of evolution, based on the conclusions of Dr. J. C. Willis, F. R. S. *Philosophical Transactions of the Royal Society of London B* **213** (1925), 21-87. https://doi.org/10.1098/rstb.1925.0002.