Preface

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The year 2009 had two important scientific celebrations: "The International Year of Astronomy" and the "Darwin Year". In Astronomy, four hundred years had passed since the first use of the telescope by Galileo Galilei and publication of the first two planetary laws by Johannes Kepler in the book Astronomia nova, published in Prague in 1609. In Biology, the bicentennial of Darwin's birthday and the sesquicentennial of the publication of his book *The Origin of Species*, published in London in 1859, are two important ephemerides of what is now commonly known as the theory of evolution [1]. However, 1809 was also the year of publication in Paris of the book *Philosophie zoologique*, by Jean-Baptiste Lamarck [2], containing an outline of the theory of evolution, although without the key concept of natural selection that was proposed later by Charles Darwin and, independently, by Alfred Russell Wallace.

Darwin's classical book had the great merit of showing that the organization and functionality of living beings comprise a natural process that Science can explain, but which in no sense had a single mathematical model. Nothing vaguely similar to an equation appears on any page. But Darwin respected mathematicians and even once said "I have deeply regretted that I did not proceed far enough at least to understand something of the great leading principles of mathematics; for men thus endowed seem to have an extra sense" (quoted in [3]).

Also around one and a half centuries ago, Gregor Mendel, an Austrian monk and scientist, was studying the reproduction of peas in Brno, a city that is now in the Czech Republic. His work, in which statistics played a central role in predicting how traits were inherited from one generation to the next, led to the formulation of what later became known as Mendel's Laws of Inheritance, which were published in 1866 [4] but were rediscovered only at the beginning of the 20th century. What Mendel devised was the "mechanism of heredity" that was lacking in Darwin's theory. Until then, it was assumed that offspring were a blending of their progenitors. This would make evolution impossible, as variation would very quickly disappear from any population. This was a fundamental objection to Darwin's theory and, as it was only lately recognized, Mendel's laws formed not only the foundation of the modern science of genetics but also found the missing link that made the theory

of evolution a mature one, since it is a key ingredient for differential reproduction and, therefore, selection and evolution.

The so-called "Modern Evolutionary Synthesis", made possible only by the active intervention of a generation of great biologists with fundamental training in mathematics and physics, like Ronald A. Fisher, John Haldane, and Sewall Wright, among others, succeeded in merging Darwinian evolution and Mendelian genetics. In fact, the need to make the theory of evolution by natural selection explicitly quantitative was advocated by British biometricians, with the development of statistics as an area of mathematical enquiry, that led to creation of the journal *Biometrika*, by Pearson, Weldon and Galton (cousin of Darwin) in 1901. But that synthesis, in which the fundamental concepts of evolution, selection and mutation were formulated in terms of a mathematical model, took place only in the 1920s and 1930s. An important development in biological modelling with a strong mathematical background that is also worth mentioning was the formulation of a neutral theory of evolution, by Motoo Kimura [5] in the 1960s, in which the vast majority of evolutionary change at the molecular level is caused by random drift of selectively neutral mutants. A second important development was the introduction of evolutionary game theory in Biology, by John Maynard Smith [6] in the mid-1970s, in which the replicator and the replicator-mutator equations play a fundamental role, in particular, giving origin to "Darwinian Dynamics" or "Evolutionary Dynamics" as a mathematical description of the dynamical process of variability, heritability and the struggle to survive and reproduce that underlies natural selection [3, 7].

This briefly sketched story, is, in a certain sense, the starting point of this book; however, this was not the starting point of the relationship between mathematics and biology nor does it cover the whole field of Mathematical Biology, which includes many topics such as population dynamics, theoretical ecology, epidemiology, population genetics, theoretical immunology, neural networks, pattern formation, and genomic or proteomic analysis. That story is in fact much older. However, it is difficult to establish the beginning of this interaction. One of the first references is from the 13th century, when Fibonacci's rabbit problem was formulated in 1202: "Suppose a newly-born pair of rabbits, one male, one female, are put in a field. Suppose that our rabbits never die and that after the first month, females always produce one new pair (one male, one female) every month from the second month on. How many pairs of rabbits will there be after a certain number of months?" The assumptions are so unrealistic that this problem hardly can be considered a problem in biomathematics; actually, it appears as an interesting example of certain mathematical recursion [8]; however, the Fibonacci sequence plays an increasing role in the description of nature.

Despite the fact that Darwin was influenced by Thomas Malthus' "An Essay on the Principle of Population", first published in London in 1798, the model of population growth following a geometric progression was already well known by the mathematician Leonhard Euler. Already in the 18th century he discussed several examples of dynamics of human population and he understood that they

correspond to a model of exponential growth [9, 10]. Working with this model, he was able to observe, fifty years before Malthus, that a single couple, living only several hundreds of years ago, was able not only to generate all the human population at the 18th century but also, continuing with the same growth, even to attain so large a total population that the whole Earth could not be fed. He also contributed a chapter to a second edition of a first treatise on demography published in Berlin in 1761.

In an important memoir presented to the Academy of Science of Paris in 1760, Daniel Bernoulli made what is possibly the first use of modern mathematical techniques to solve a biologically relevant problem: the dynamics of smallpox. Bernoulli was ahead of modern epidemiology and divided the population into two categories: the susceptible and the immune (the survivors gain life-time immunity); these groups were modelled using differential equations. In fact, in his model he obtains and solves what we nowadays call a "logistic equation", which is a particular case of Bernoulli's differential equation, named after his uncle Jakob, who discussed it in 1695. Looking at the stationary states of these equations, he was able to project the loss in life-expectancy due to the disease. This had impact in the insurance market, and was also a central question in the introduction of inoculation in France [11].

Population dynamics is one of the most important fields of biomathematics; almost all books on the subject start with a chapter on that topic. We still call "Leslie matrices" the one introduced in the study of structured populations, despite the fact that they have no special attributes from the mathematical point of view [12]. The same thing happens with the (sometimes called) Verhust equation [13], which is just the logistic differential equation already considered and solved by the Bernoullis and is one of the simplest examples of a dynamical system. Perhaps the same cannot be said about the Lotka-Volterra equations, introduced almost simultaneously in 1925 and 1926, respectively, by the American statistician A.J. Lotka and the Italian mathematician Vito Volterra, that describe the interaction between different species and gave rise to a turning-point in mathematical biology in the 20th century, [14]. Other interesting facts with historical references to the interactions between mathematics and biology can be found in [15].

The first mathematical result of interest in evolution and genetics appeared only decades after Darwin. In the first decade of the 20th century, independently, the British mathematician G.H. Hardy [16] and the German doctor W. Weinberg [17] explained why recessive genotypes do not disappear. More precisely, they gave sufficient conditions to make gene frequencies static from one generation to the next. In their ideal model, an equilibrium is attained in a single generation. The knowledge of equilibrium is the baseline against which we can measure change, and evolution is ultimately a theory of (gene frequency) change. Their conditions were no-mutation, no-selection, no-migration, random mating, infinite population. The violation of any of these conditions could, on its own, be responsible for evolution.

Later on, R. Fisher [18] went further and quantified the change, pronouncing what is currently known as "the fundamental theorem of evolution": the rate of

change of the mean fitness of a population is equal to the fitness variance at each point in time. This will be discussed in detail in the chapters of this book written by W. Ewens, P. Schuster, and R. Burger. These first three papers will provide the reader with a broad and deep view of models in population genetics.

The book continues with a chapter by P. Jagers studying models for extinction. The starting point will be the Galton-Watson process, initially introduced in the study of extinction of family names. This shows (if someone is not yet convinced) the unifying nature of mathematical knowledge. P. Taylor presents the relations between group theory and homogeneous populations. This provides a consistent framework for generalisation to an entire population of results obtained by studying only one or a few (focal) individuals. Taylor finishes his chapter with a model of altruistic behaviour. This is the starting point of the following chapter, by J. Pacheco, where evolutionary game theory is intensively used to model collective action (in particular, cooperation). Solutions of social dilemmas are probably one of the most important problems we have to face in our daily life.

Yet, there are many different ways to study the evolution of cooperation; two important ones are kin selection and group selection. These models are reviewed and used in V. Jansen's chapter to provide a full understanding of the social behaviour of mice living in haystacks. When different individuals in the same population find different solutions to the same dilemma, we are possibly facing one of the most important problems in evolution: the concept of speciation. So important that the title of Darwin's masterpiece refers directly to it. This is the subject of the chapter by S. Mirrahimi, B. Perthame, E. Bouin and P. Millien and also of S. Méléard's chapter. Models for evolutionary branching, a more general concept, are studied from many different points of view: differential equations, integro-differential equations, stochastic modelling, individual-based models, asymptotic limits... all approaches unified by the concept of "adaptive evolution".

"Adaptive evolution" is also the topic of the last two chapters, respectively, by H. Metz and by M. Gyllenberg, H. Metz and R. Service. These chapters are primarily devoted to meso-evolution, where the focus is the change of traits of individuals in a population. A natural sequel to Metz's chapter, where some elements of an adaptive evolution theory are developed, this final chapter investigates how optimisation approaches fit that point of view.

The book ends with a large and extensive but not exhaustive, bibliography, a merging of all citations that appear in the book. At a first glance, this allows us a rather reasonable overview of the biomathematical literature in the last 150 years. We intend this book to be also a good starting point for anyone interested in working in biomathematics, especially in evolution.

where the conference took place in November 2009, to reunite the scientific and logistic conditions that made this book possible.

Finally we conclude this introduction by adopting Metz's closing sentence and inviting you, interested reader, to join this hard and challenging task of bringing Biology and Mathematics closer and to contribute to the fruitful development of biomathematics!

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