Book Review

Population Genetics – A Concise Guide by John H. GILLESPIE

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Second Edition

Climbing the moving mountain?

I would like to hazard a guess that a large proportion of molecular biologists, if not a majority, when presented with a piece of research that contains an evolutionary term or an algebraic equation will either scan over it, accepting it as a truism, or shuffle uncomfortably in their chair, try hard to grasp the meaning, and then move on to more familiar territory. It is the regrettable reality that mathematics tends to have a polarizing effect on people's enthusiasm, even unfortunately on scientists. And yet in order to understand the essence of a subject we all hold dear – evolution – a firm grasp of the mathematics is unavoidable. With this in mind 'Population Genetics' attempts very successfully to try and ease as gently as possible the timorous reader into this mathematical and model-bound subject, and allows us after some degree of effort, as the author puts it, to "enjoy the experience of understanding what was previously mysterious." The book, concise though it is at 214 pages, is disconcertingly an expanded version of an original of only twenty-one pages, and yet the idea behind both formats was to present the fundamental ideas or core topics in population genetics, and equip the reader such that "the rest of population genetics should be approachable." The only requested prerequisites for tackling the text are an understanding of Mendelian genetics, molecular genetics, simple algebra and elementary probability theory. Reading it can be done at two speeds, one delving into the mathematics and solving the problems given after each section, or two, just trusting the equations provided (a habit the book should wean us off) and limiting oneself to the conclusions drawn.

The first and most important concept we are introduced to is "The Great Obsession" or in the vernacular – what are the forces that lead to the observed divergence between individuals of the same species? In chapter one, we are reminded of the universality of the Hardy-Weinberg Law and the sturdiness of the equilibrium as observed in outbreeding populations, after which the concept of genetic drift and the Wright-Fisher model are introduced. A bag of marbles and a few equations later, and we realize the results genetic drift are never repeatable – alleles being lost with no systematic tendency. We find out, with some degree of relief, that would take 1.38 million generations to halve the variation in a population of one million individuals: conflict between genetic drift and Hardy-Weinberg is avoided because of the different time scales at which they act; theoretical descent into a homozygous world caused by drift is prevented by mutation. Kimura and Ohta's classic paper of 1971 on neutral theory is analyzed in detail to include the subsequent problems in its validation. Leaving the simpler theories, chapter three then introduces us to relative fitness and natural selection, examining the familiar cases of the European scarlet tiger moth and sickle-cell anaemia, the latter being on theoretical grounds a very unusual case of overdominance. The inverse homozygous-heterozygous effect of Greenberg and Crow, and how fluctuations in the environment drive changes in fitnesses that then lead to stable polymorphisms are deftly explained.

At times the mathematics only seems to be restating the obvious, and yet at others the results extracted come as a pleasant surprise. For example, the probability of fixation of an allele is 99% when there are 4605 alleles, irrespective of the population size (when the selection coefficient s is = 0.001). The theory reveals a brutal truth, "(the) critical time for a new mutation is between its creation and its increase to a relatively small number of copies." At this point in the proceedings, natural selection and genetic drift can then be pulled together and four models of molecular evolution squeezed out – neutral, positive, negative and changing environment. As if to soothe the reader from the effects of a synthesis of concepts followed by its fragmentation, the author goes on to question the validity of the four models, and even recommends the reader should try and grapple with improved versions.

Halfway through the book, in the fourth chapter, we are then lured to the ideas of linkage disequilibrium, hitchhiking and genetic draft (as opposed to genetic drift) with a carrot in the familiar form – at least for molecular biologists – of genomic sequences and bioinformatics. According to the information obtained from the mass of sequence data being accumulated, in loci close to the telomere and centromere there is a reliable positive correlation between rates of recombination and the degree of silent variation. In order to explain this observation, Begun and Aquadro, in 1992, were able to demonstrate that rates of substitution in the X chromosome of *Drosophila melanogaster* were about the same in both regions of high and low recombination, thereby excluding the hypothesis that mutation rates are correlated with recombination sites. The accepted theory is that as a single mutation is selected for, those alleles at closely linked loci will be carried over (hitchhiking) until they are eventually released by recombination. In the absence of recombination, linked alleles are fixed and genetic variation is eliminated. The process of hitchhiking can be divided into initial random and subsequent deterministic phases. Genetic draft, the random component, is shown to be potentially a more important force within natural populations than its cousin drift. Passing on to chapter five, we then return to Hardy-Weinberg, but under conditions of non-random mating, where the effects of inbreeding are considered. In a section devoted to the evolution of selfing in plants, we discover that the mean fitness of a selfing population decreases initially; however, as selection weeds out those mutations that are deleterious, the mean fitness of the population is in fact higher than that of a comparable outbreeding population. As an interesting side point, the only thing that stops us humans becoming selfers is that we have a higher coefficient of inbreeding than that of plants, which means that our inbreeding depression would be too great to allow for the evolution of selfing.

Heritability, covariance and dominance are amply covered in the quantitative genetics chapter, along with a somewhat academic though necessary delve into selective breeding. The final chapter deals with the evolution of sex, the importance of synergistic epistasis and how Muller's rachet works both on paper and in the Y chromosome.

In general the algebra is well explained, but at times, depending on one's background, can be quite dense, especially in the latter half of the book. Nevertheless, it is always presented stepwise and regularly interspersed with informal comments which keep it convivial. The claim is that the algebra is of a level to be found in high school courses, with a few exceptions that are included in the appendices, but does everyone have a fresh recollection of their high school history course? One other minor negative, for the sake of carping, would have to be the dispersal of problems throughout the text, which though aimed clearly to punctuate themes, can be at times distracting. The author is gentle with the reader, and maintains a familiar degree of self-criticism which allows the reader to get caught up in the author's enthusiasm for the subject and gives a sense that he's not just preaching. His informality is refreshing and his constant minor digressions into the non-algebraic world a welcome break. Evolution, even at this 'core' theoretical level can be a challenging subject for the uninitiated, and to get a full grasp of all the concepts requires a fair share of effort; being then asked to "imagine climbing a mountain that keeps moving…" as a metaphor for evolution somehow makes the effort all the more enjoyable.

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