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QUANTIFYING INTROGRESSION RISKS WITH HAZARD RATES

INTRODUCTION

Introgression is the permanent incorporation of genes from the genome of one population into that of another through hybridisation and backcrossing. With the advent of genetically modified (G.M.) crops, the potential that such transgenes might introgress from cultivated to wild plants has become a point of scientific scrutiny. Ellstrand et al. [1999] found that 12 out of the 13 most important food crops in the world hybridise readily with wild relatives, which suggests that the potential for introgression is certainly there. There are multiple and diverse consequences of such gene flow, from the genetic assimilation of crop genes and resulting loss of wild biodiversity [Haygood et al., 2003], to the creation of herbicide-resistant weeds [Owen and Zelaya, 2005]. The discussion of the possible consequences of introgression is beyond the scope of this work. Instead I would like to consider how one should answer an equally fundamental problem of introgression: what is the chance that it occurs, and if it does occur, when is this most likely to happen? This thesis provides a theoretical framework which helps to answer these questions.

Previous model-based studies of introgression are largely deterministic. The number of hybrids appearing in a wild population might initially be small. Consequently, stochasticity in the number of offspring of invaders (demographic stochasticity) is a crucial aspect of introgression, which has been neglected in much previous work [Davis et al., 1999, Thompson et al., 2003]. Also, little work has been done on defining when introgression actually occurs. For example, Thompson et al. [2003] investigates the number of individuals carrying a foreign gene, and considers that introgression has occurred when this number crosses some threshold. The choice of this level is arbitrary, which makes this approach unsatisfactory.

A quick thought experiment suggests that introgression is inevitable if there is a recurrent gene flow of some fitness-enhancing gene from crops into wild populations. If a single invader has some probability (however small) of initiating a successful invasion into a population, then a flow will almost surely result in a successful lineage becoming established eventually. This is not to say that the risk of introgression is high—even though a successful invasion will eventually occur, it might still take a long time, so the risk of introgression might be acceptably small. Thus, the key to calculating introgression risks lies first in finding the distribution of times at which invasions occur. After this is done, an appropriate measure of introgression risk can be calculated.

A quantity known as the hazard rate is a strong candidate for such a risk measure. The hazard rate of an event is defined as the probability per time unit that the event occurs given that it has not previously occurred. Aside from being an appropriate quantitative measure, hazard rates also provide an intuitive

basis for understanding the risk of events. For example, the hazard rate of an individual winning the weekly lottery is simply the probability per week of winning the lottery (given that the individual has not won the lottery before). Note that the hazard rate can change in time, e.g. a lottery player might buy multiple tickets during some weeks, but buy none at others. Hazard rates have been used widely in the field of survival analysis [Kalbfleisch and Prentice, 2002, for example]. Once the hazard rate has been calculated, then factors affecting introgression risk, and effective risk mitigation strategies can be devised. The hazard rate can be calculated from stochastic models of the introgression process. In this thesis, we use branching process models to do so. For the interested reader, Haccou et al. [2005] provides an introduction to the use of branching process in biology.

The overall aim of quantifying introgression risk must involve combining appropriate theoretical and experimental procedures. The theoretical work within this thesis should be seen as one of three sub-projects with a common goal. The aim of the overall project is to use the carrot (*Daucus carota*) as a case-study in developing a methodology to quantify introgression risk. One sister sub-project investigates short term introgression incidence by crossing several cultivars and wild plants. The results from these crossing experiments can be combined with the results contained within this thesis to estimate introgression risks. Long term introgression incidence is studied by another sub-project, which uses molecular markers to estimate past levels of introgression. The results from studying the molecular markers can be used to validate the predictions from the crossing experiments and theoretical approaches. The whole project benefits from an interdisciplinary collaboration between several members from the Institutes of Biology (IBL) and Environmental Sciences (CML) of Leiden University, and is funded by the Netherlands Organisation for Scientific Research (NWO) as part of their research program 'Ecology Regarding Genetically Modified Organisms' (ERGO).

One of the characteristics of introgression is the occurrence of repeated invasions, each with a small probability of success. Furthermore, changes in fitness of individuals carrying the invading gene may occur, due to changes in the genetic background of the gene. Similar processes occur in many other contexts. For example, the spread of invasive species into new territories, or the invasion of a disease from one host species to another. Consequently, I hope the methodologies and results which follow prove of use to researchers across a range of fields.

Chapter 1 introduces the general methodology for calculating hazard rates of introgression using a time-homogeneous model of monocarpic perennials with an age-structure. The paper explains how deterministic methods cannot be used to calculate hazard rates. In addition, it proves the monotonic increase of the hazard rate with time for all time homogeneous models, investigates the effect of variance on invasion risk, finds that the hazard rate can either increase or decrease with flowering probabilities, and shows how Taylor approximations of branching processes can lead to biologically plausible arguments.

Chapter 2 uses a special case from chapter 1 in combination with preliminary results from empirical studies to investigate the hazard rate of introgression from cultivated carrots into their wild relatives. A sensitivity analysis of key life-history parameters is performed, and the results are explained in terms of assumptions and results from chapter 1.

Chapter 3 investigates the effects of including deterministically varying environments in introgression. Deterministic changes could be human-mediated and used in management strategies for risk mitigation. In particular, it focusses on deterministically varying hybridisation rates on the hazard rate, in scenarios such as crop rotation. In such models, the hazard rate changes with time. Procedures for finding a constant hazard rate which approximates the time-changing hazard rate are given. Also, chapter 1 assumes that all backcrosses have identical life-history parameters, and these assumptions are relaxed in chapter 2.

Chapter 4 presents procedures for incorporating multiple loci and alleles into hazard rate calculations. It shows how the linkage of a transgene to some quantitative trait locus can affect the hazard rate. In addition, it is shown how to calculate hazard rates using computer simulations as well as from branching processes. In previous chapters it was necessary to assume that introgression was occurring into a large wild population to maintain mathematical tractability, but the question remained as to how large was large enough. The use of computer simulations allows us to answer this question, and we find that branching processes do indeed provide a good basis for calculating invasion risks at ecologically realistic population sizes.

Chapter 5 extends the methodology to include introgression in random environments. In such scenarios, as in chapter 2, the hazard rate conditioned on the environment changes with time. It might be tempting to take the mean hazard rate as a risk measure, but this chapter shows that this would mean that introgression risks might be grossly underestimated at some times. Contrary to previous studies, we find that randomly changing environments can either increase or decrease introgression risks when compared to predictions from models with time-homogeneous parameters.

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