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Applications Note

Genetics and population analysis

QuantiNemo 2: a Swiss knife to simulate complex demographic and genetic scenarios, forward and backward in time

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Abstract

Summary: QuantiNemo 2 is a stochastic simulation program for quantitative population genetics. It was developed to investigate the effects of selection, mutation, recombination and drift on quantitative traits and neutral markers in structured populations connected by migration and located in heterogeneous habitats. A specific feature is that it allows to switch between an individual-based full-featured mode and a population-based faster mode. Several demographic, genetic and selective parameters can be fine-tuned in QuantiNemo 2: population, selection, trait(s) architecture, genetic map for QTL and/or markers, environment, demography and mating system are the main features.
Availability and implementation: QuantiNemo 2 is a C++ program with a source code available under the GNU General Public License version 3. Executables are provided for Windows, MacOS and Linux platforms, together with a comprehensive manual and tutorials illustrating its flexibility. The executable, manual and tutorial can be found on the website www2.unil.ch/popgen/softwares/quantinemo/, while the source code and user support are given through GitHub: github.com/jgx65/quantinemo.
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Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

With the recent flood of genomic data and the fast increase of computer power, simulating the evolution of traits and their underlying genetics plays an increasing role in evolutionary genetics and population analyses. The number of programs available to perform such simulations is also increasing and allows to choose from a large set of tools with varying levels of complexity when starting a new project. A list of available software is given in Hoban *et al.* (2012), while Peng *et al.* (2013) built a comprehensive website (https://popmodels.cancercontrol.cancer.gov/gsr/) where they present the comparisons of various existing genetic and genomic simulation software. As pointed out by both Hoban *et al.* (2012) and Peng and Kimmel (2005) all of these programs have limitations. In individual-based programs, software are in general limited to predefined scenarios (Guillaume and Rougemont, 2006), or require knowledge of a programming language (Peng and Kimmel, 2005).

Most population-based programs, on the other hand, are limited to simple demographic scenarios (Excoffier *et al.*, 2013; Hudson, 2002). Some exceptions exist but are in general limited to simple models. For example Ray *et al.* (2010) offers only 2 D stepping stone as a dispersal model and the population can only be regulated logistically.

In their review, Hoban *et al.* (2012) acknowledge that quantiNemo 1 (Neuenschwander *et al.*, 2008) was the software package with the highest degree of flexibility. The new quantiNemo 2 offers even more flexibility to the user: The number of parameters

has doubled, allowing exploring a larger variety of situations without any need of programming skills. To improve efficiency, the possibility to switch from individual-based to coalescence-based simulation, within one run of the program has been incorporated.

2 General features of quantiNemo

QuantiNemo allows simulating realistic population dynamics with various population growth models (constant population, logistically regulated, exponential, etc) and dispersal models (1 D stepping stone, 2 D stepping stone, island, etc). Every individual carries a genome formed by an arbitrary number of loci placed on a genetic map. Each locus can be either neutral or contribute to a quantitative trait with several mutational models as options. Each quantitative trait has its own specifications. The trait determinism can be purely additive or include dominance and/or epistatic interactions among loci. Moreover, several mating systems are available.

3 New features of quantiNemo 2

3.1 Coalescence

To simulate larger population size over longer time period, QuantiNemo 2 offers the possibility to switch from individual-based to population-based simulation with coalescence. To implement the coalescence algorithm, a forward-in-time, population-based simulation first simulates any complex demographical scenario, followed by a backward-in-time coalescence simulation. This setup allows for much more elaborate scenarios than common coalescence tools, including modelling isolation by distance and long-distance dispersal. The coalescence tree can be constructed for the entire population using exact coalescence (where multiple coalescence events can happen in one generation) or for a subsample of the population, where approximations are used allowing to speed-up simulation. This allows, for example, inferring a demographic history using efficient population-based simulations and then to make the simulations more realistic by switching to individual-based simulations where selection can be simulated.

3.2 Sex chromosomes

QuantiNemo 2 allows for the sex of an individual to be determined genetically. Together with the genetic map which may differ for male and female, this allows to simulate various type of sex chromosomes (e.g. XY or ZW system). Sex may not only be determined genetically, but may also be determined entirely or partially by the environment, e.g. temperature-dependent sex determination.

3.3 Fitness landscape

QuantiNemo 2 offers the possibility to simulate fitness landscapes of any shapes and thus any number of optima. This means that an arbitrary fitness can be assigned to each phenotype. This is particularly relevant when epistasis is present and allows to associate a given fitness to any genotype, thereby simulating a wide variety of scenarios.

QuantiNemo 2 has also been greatly improved in terms of flexibility of use (new statistics, new macros, possibility to sub-sample populations or restart simulations).

Other new features are a new mating system (cloning), new population growth models, corrected and more realistic density-dependent dispersal rates. The genetic map can now evolve with time and the distance between loci can accommodate quantitative traits using recombination factors, and the genotypes can now be exported as Arlequin files (Excoffier and Lischer, 2010) or PLINK files (Purcell *et al.*, 2007). Moreover, a large variety of tutorials has been developed to guide new users.

For an exhaustive list of all features, please see the manual.

4 Examples

QuantiNemo 1 has been used in a variety of contexts. For an exhaustive list of examples please see Supplementary Materials.

QuantiNemo 2 is born with specific user needs in mind and a pre-release version of quantiNemo 2 was used in various publications. For example, Kanitz *et al.* (2018) simulated the spread of humanity from East Africa to the entire world. This required simulating up to five million individuals over a period of about 132 000 years for a large set of varying parameters (migration rates, population growth rates, etc). Such large-scale simulations can only be performed using coalescence. To the best of our knowledge, no other coalescence simulation tool provides as much freedom to simulate such complex pattern of dispersal and growth as quantiNemo 2. Antoniazza *et al.* (2014) used a similar approach to simulate the recolonization of Europe by barn owl after the last glaciation. Cavoto *et al.* (2018) used new features of quantiNemo 2 related to the sex chromosomes. The authors showed that the interplay between sex-antagonistic genes and deleterious mutations can lead to the maintenance of recombination on the sex chromosomes, preventing the degeneration of sex chromosomes. They also explored the expected parameter range of such a maintenance, thereby gaining a better understanding of the diversity of sex-chromosomes observed in nature.

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