Simulation and analysis of evolutionary models of cancer progression and adaptive therapy

Offer

Introduction: What we do

We work on developing and comparing methods to understand **restrictions in the order of accumulation of driver mutations in cancer**, using oncogenetic trees and related approaches, and how they can be used to **predict tumor evolution**. We evaluate these methods using explicit **evolutionary models of tumor progression**, and we have also started focusing on how they can be used to design **adaptive therapies**, as well as how interpretation is affected by **frequency dependent fitness**.

Developing general-purpose software for evolutionary simulations of tumor progression (and, more generally, clonal evolution) is a key element of that workflow. We have developed code for that purpose using C++ which is called from R (using Rcpp) and I want to extend this code to add new functionality and make it much more flexible and versatile as well as faster; this includes exploring additional algorithms and languages. Your work could focus on the implementation and development of evolutionary simulations of tumor progression. It might instead involve analyzing data to examine the consequences of different evolutionary models of tumor progression, including different cooperation regimes, or the consequences on tumor progression of different therapeutic intervention regimes; the data to be analyzed would be mainly data simulated by us from known evolutionary models and fitness landscapes, but possibly also "real" data from the literature. Or it could involve extending and improving some R and web applications we have developed (evamtools).

Possible projects

We would discuss the details of the specific projects depending on your interests and skills. As an example, these are some topics we could address:

- Implementing additional models of population growth and additional algorithms for stochastic simulation.
- Understanding the role of frequency-dependent fitness on models of cancer progression.
- Simplifying and integrating the newly available options (spatial models, frequency-dependent fitness, interventions) in the simulation code.
- Using classification (machine learning) approaches to identify when methods can/cannot be applied to a given data set.
- Conducting simulation studies under appropriate null models to assess the performance of methods to identify restrictions.
- Examining the consequences of different intervention regimes (adaptive therapy) on tumor progression.
- Using Julia (https://julialang.org/) and Julia with C++ instead of R (with C++) as the main language for the simulations.
- Developing a web-based interface for the simulations (using R or Julia or Racket or ...).
- Rewriting some of the core simulation code in C++ to use GPUs.
- Extend the functionality and improve the workings of our Evam-tools web app and R package (https://www.iib.uam.es/evamtools/ and https://github.com/rdiaz02/EvAM-Tools).

References:

Evam-tools: https://www.iib.uam.es/evamtools/ and https://github.com/rdiaz02/EvAM-Tools

Diaz-Colunga, J, Diaz-Uriarte, R. 2021. Conditional prediction of consecutive tumor evolution using cancer progression models: What genotype comes next?. PLoS Computational Biology (https://doi.org/10.1371/journal.pcbi.1009055)

Diaz-Uriarte, R, Vasallo, C. 2019. Every which way? On predicting tumor evolution using cancer progression models. PLoS Comp Biol (https://journals.plos.org/ploscompbiol/article?id=10.1371/

journal.pcbi.1007246)

Diaz-Uriarte, R. 2018. Cancer Progression Models And Fitness Landscapes: A Many-To-Many Relationship. Bioinformatics (https://doi.org/10.1093/bioinformatics/btx663)

Diaz-Uriarte, R. 2017. OncoSimulR: genetic simulation with arbitrary epistasis and mutator genes in asexual populations. Bioinformatics. https://academic.oup.com/bioinformatics/article/2982052/OncoSimulR: (OncoSimul package repository: https://github.com/rdiaz02/OncoSimul)

Requirements:

- Depending on the specifics of the project:
  - Strong programming skills.
  - Good working knowledge of R.
  - Knowledge of C++.
  - Knowledge of (or interest in) Julia.
  - Knowledge of (or interest in) evolutionary biology.
  - Knowledge of parallel computing.
  - Knowledge of GPGPU computing.
  - Knowledge of (or interest in) statistics, including causal inference and adaptive treatment regimes.

- Experience using Linux/Unix.

- Having taken a look at the "References" to make sure you are really interested. :-))

(The above are not "hard requirements", so talk to me if you are very interested in the project but you feel that currently you do not fulfill the requirements.)

Contact

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