Summary

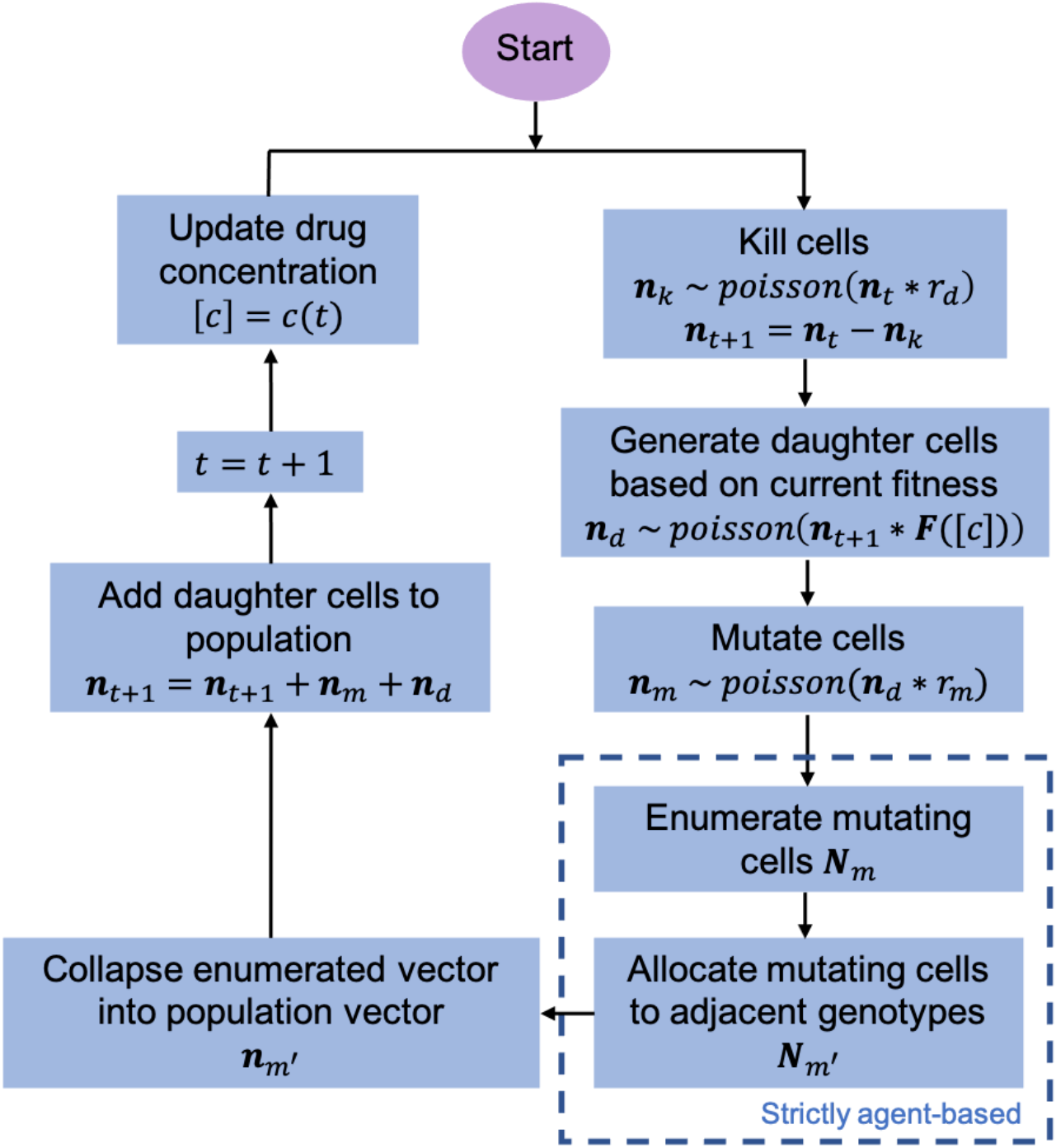
The evolution of drug resistance across kingdoms, including in cancer and infectious disease, is governed by the same fundamental laws. Modeling evolution with genotype-specific dose response curves, collectively forming a 'fitness seascape', enables simulations that include realistic pharmacokinetic constraints, more closely resembling the environmental conditions within a patient. FEArS (Fast Evolution on Arbitrary Seascapes) is a python package that enables simulating evolution with fitness seascapes. FEArS can simulate a wide variety of experimental conditions with many arbitrary biological parameters. FEArS remains computationally efficient despite being an agent-based model, even for very large population sizes. FEArS also contains powerful and flexible utilities for data analysis, plotting, and experimental fitness seascape estimation.

A hybrid agent-based algorithm

FEArS achieves fast runtimes while simulating large populations of evolving agents by employing what we term a 'hybrid agent-based' approach. When possible, populations are stored as vectors of cell numbers $\hat n$, where each position in the vector corresponds to a genotype and the number at that position gives the number of cells of that type in the population. Then, stochastic events such as cell division and cell death are simply drawn from poission distributions:

\begin{equation}\label{eq:cell_death} \hat n_{d} ~ poisson(r_{d}*\hat n), \end{equation}

where $\hat n_{d}$ refers to the vector of dead cells of each type, for example. However, in the mutation step, FEArS switches to a strictly agent-based process. Here, every mutating agent is enumerated in a vector, where each entry in the vector represents the genotype of the agent. Then, mutating agents are randomly allocated to adjacent genotypes.



Statement of need

FEArS enables stochastic simulations of clonally evolving systems subject to arbitrary drug concentrations over time. By using an agent-based algorithm, we are able to model mutation and selection, with evolution arising as an emergent phenomena. Furthermore, by allowing for arbitrary population sizes, FEArS can model population extinction. Arbitrary population sizes allows us to simulate how a disease population within a patient may respond to therapy. In addition, FEArS models genotype-sprecific dose-response curves, allowing for more fine-grained prediction of evolution.

Mathematics

Single dollars ($) are required for inline mathematics e.g. $f(x) = e^{\pi/x}$

Double dollars make self-standing equations:

$$\Theta(x) = \left{\begin{array}{l} 0\textrm{ if } x < 0\cr 1\textrm{ else} \end{array}\right.$$

You can also use plain \LaTeX for equations \begin{equation}\label{eq:fourier} \hat f(\omega) = \int_{-\infty}^{\infty} f(x) e^{i\omega x} dx \end{equation} and refer to \autoref{eq:fourier} from text.

Citations

Citations to entries in paper.bib should be in rMarkdown format.

If you want to cite a software repository URL (e.g. something on GitHub without a preferred citation) then you can do it with the example BibTeX entry below for @fidgit.

For a quick reference, the following citation commands can be used:

- `@author:2001` -> "Author et al. (2001)"
- `[@author:2001]` -> "(Author et al., 2001)"
- `[@author1:2001; @author2:2001]` -> "(Author1 et al., 2001; Author2 et al., 2002)"

Figures

Figures can be included like this:  Caption for example figure.\label{fig:example} and referenced from text using \autoref{fig:example}.

Figure sizes can be customized by adding an optional second parameter:  Caption for example figure.{ width=20% }

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References