

**Advanced tissue-sampling strategies**

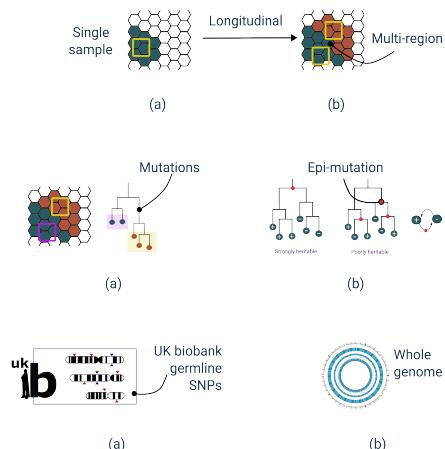
The tissue can be sampled at single (a) or multiple time-points, and in multiple spatially-separated positions (b).

**Single-cell phylogenies**

Single-cell phylogenies are generated from tissue samples (a), capturing epi-mutations with different heritability patterns (b).

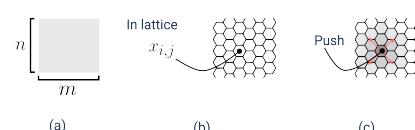
**Realistic reference genomes**

Germline reference from the UK biobank samples (a), with possibility of simulating whole-genome sequencing datasets (b).



**In lattice tissue simulation**

A tissue is a squared lattice (a), with cells positioned in a discrete coordinate system (b), and pushing each other during simulation.

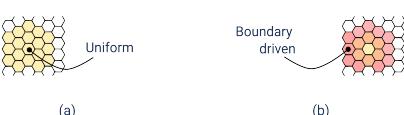


**Realistic mutational processes**

Custom rates of passenger mutations and copy numbers (a), as well as time-varying mutational processes (e.g., therapy) (b).

**Modes of cell division on the tissue**

Tissue evolution is stochastic and depends on cell parameters. Divisions happen uniformly on the lattice (a) or on boundaries (b).

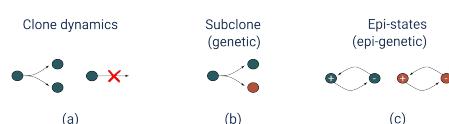


**Custom driver mutations**

Custom driver events per clone (a), as well as passenger events mapped on branches of the simulated phylogeny (b).

**Advanced birth-death process**

A stochastic birth-death process (a) with subclones that have custom parameters (b), and reversible epi-genetic events (c).

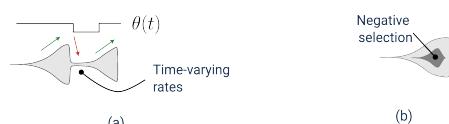


**VCF outputs**

Read-counts data in VCF format, with Beta-Binomial sequencing noise (a), bulk purity, to create variant allele frequency data (b).

**Time-varying evolutionary parameters**

The parameters of the birth-death process can vary in time to simulate therapy (a) effect and model negative selection (b).



**FASTq outputs**

SAM/FASTq outputs with a NovaSeq error model (a), which can be streamlined with standard bioinformatics pipelines (b).

