An Overview of Individual-based Simulations in Population Genetics and Cancer

Andrés Pérez-Figueroa (@anpefi)

Lab seminar

22 April 2016

GOALS

- Understand what is a simulation
- Learn how to build an Agent Based Model
- Explore how Agent Based Models had been used in cancer research

What is a (computer) simulation?

- An attempt to mimic a real-world empirical system
- The creation *in silico* of a possible world using computer programs to represent the processes under consideration

Simulations as experimental systems

- Models could be as complex as the real systems they mimic
- A huge advantage: **models are strongly manipulable**
- Simulation models are properly explored using the same experimental and statistical techniques that are used to explore real-world systems

genetic data simulation algorithms

- Backward-time (Coalescent)
- **Fordward-time**
- Resampling

Individual/Agent Based Models (IBMs/ABMs)

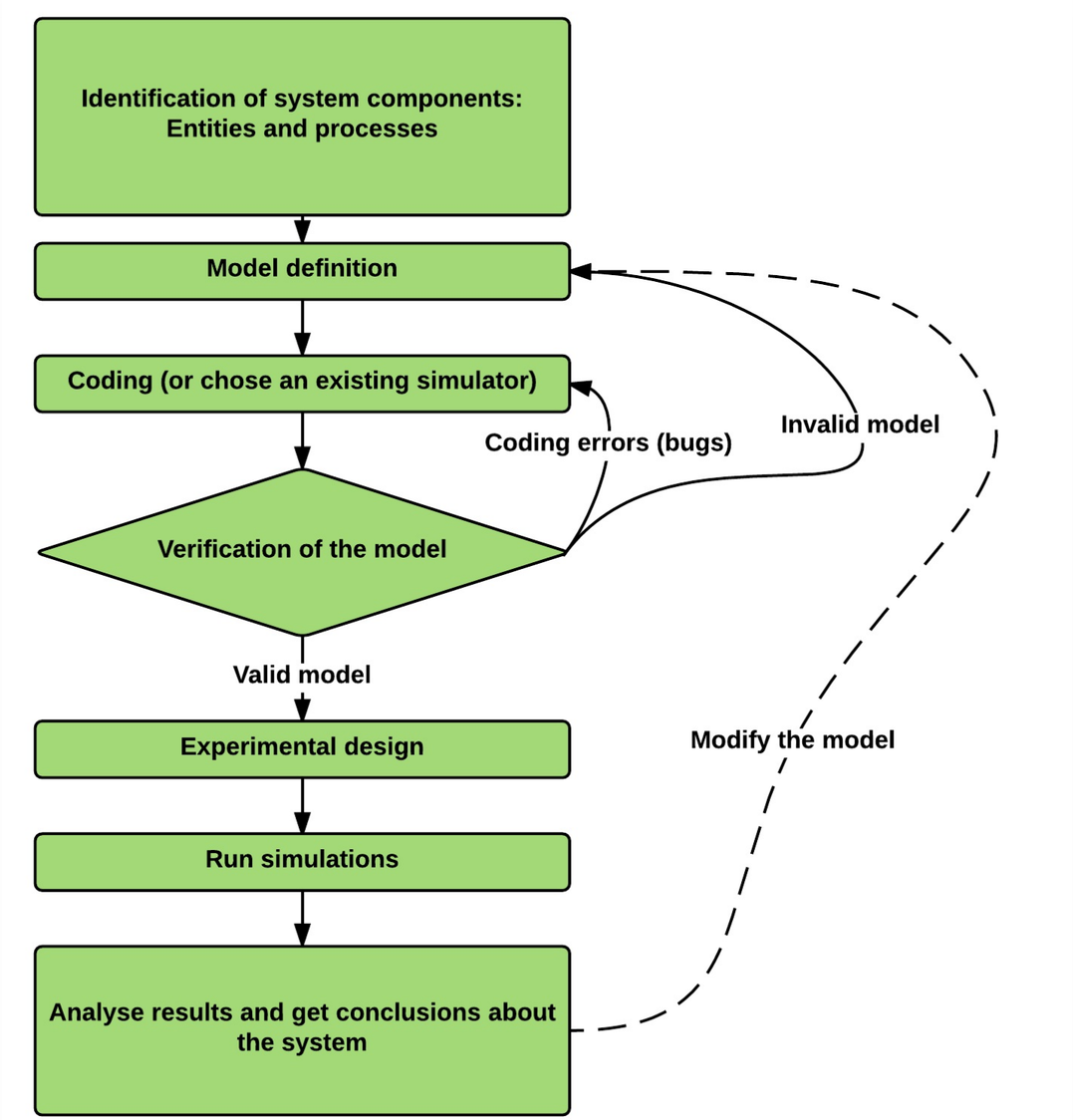
- Simulation models describing individual organisms (agents)
- How system level properties emerge from the adaptive behaviour of individuals and how the system affects individuals
- Aspects usually ignored in analytical models: individuals variability, local interactions, life cycles, ...
- More complex in structure than analytical models and then more difficult to analyze, understand and communicate

Structure of an ABM

1. A set of agents, their attributes and behaviours.
2. A set of agent relationships and methods of interaction: An underlying topology of connectedness defines how and with whom agents interact.
3. The agents' environment: Agents interact with their environment in addition to other agents.

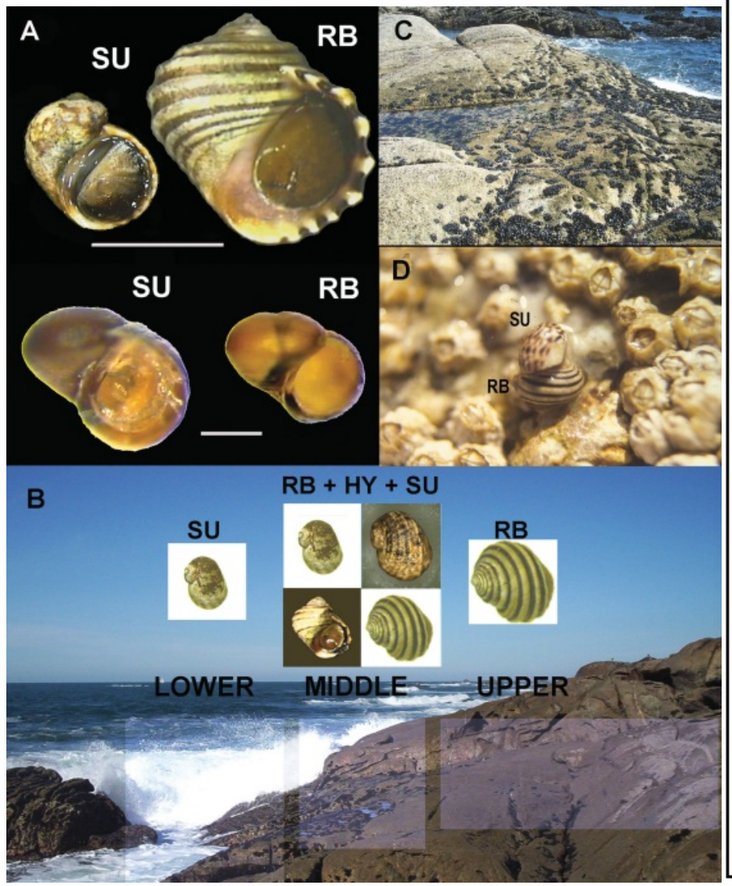
Agents repeatedly and discretly execute their behaviours and interactions.

Building a simulation study



Some Population Genetics simulators

An old example (from my Thesis)



Problema: ¿Qué fuerzas evolutivas modelan el polimorfismo observado en *Littorina saxatilis?*

Entidades:
- Poblaciones
- Individuos
- Carácter (Ecotipo)
- Cromosomas
- Loci

Procesos:
- Apareamiento
- Supervivencia
- Migración
- Asignación de fenotipo

Modelos con diversos factores:
- Aislamiento reproductivo
- Selección
- Flujo génico
- Número y tipo de loci
- Plasticidad fenotípica
- Definición de ecotipos

Programación mediante lenguaje C:
- Entidades - variables y matrices
- Procesos - funciones
- Factores - parámetros

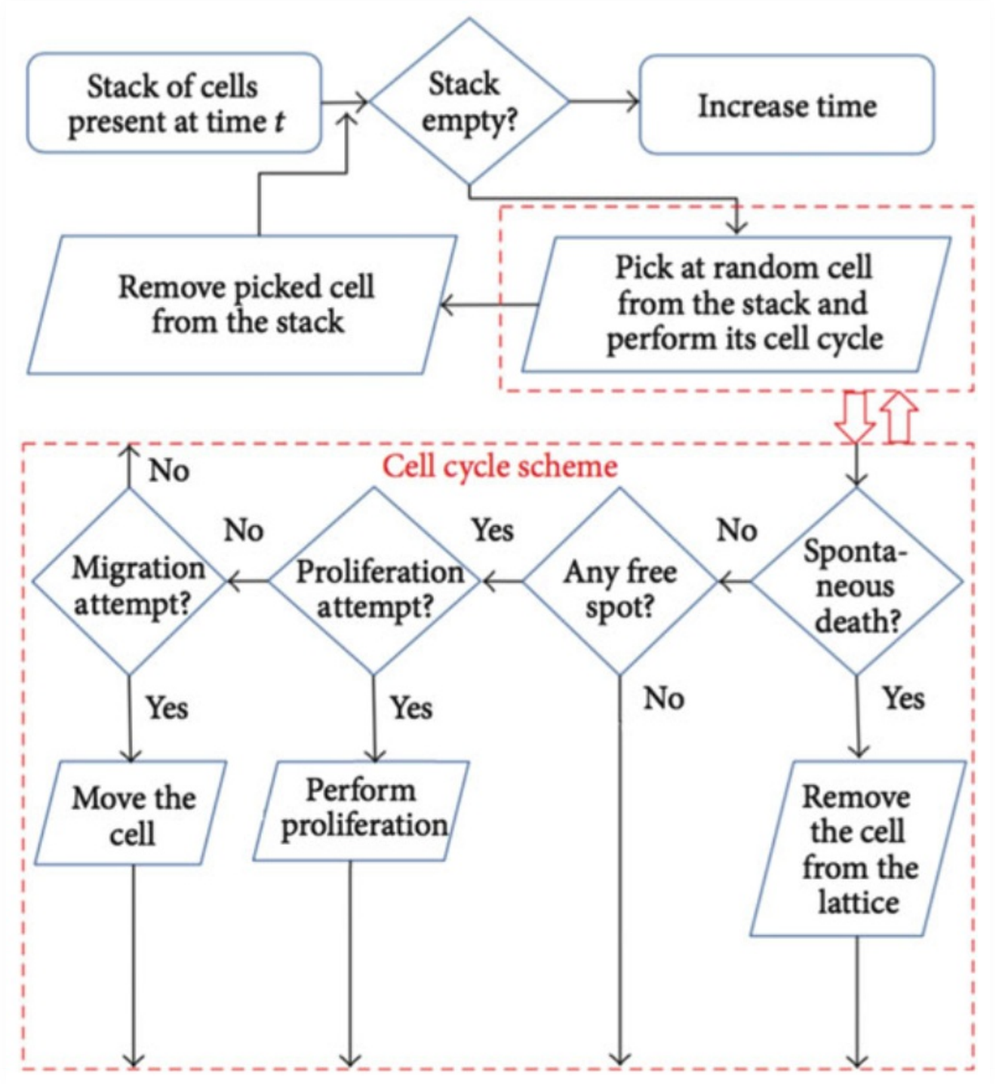
Ejecución de varios modelos posibles

Análisis de resultados:
- Comparar variables de simulaciones con valores medidos experimentalmente (índice de ajuste).
- *El modelo con menor índice de distancia explicará mejor el sistema.*

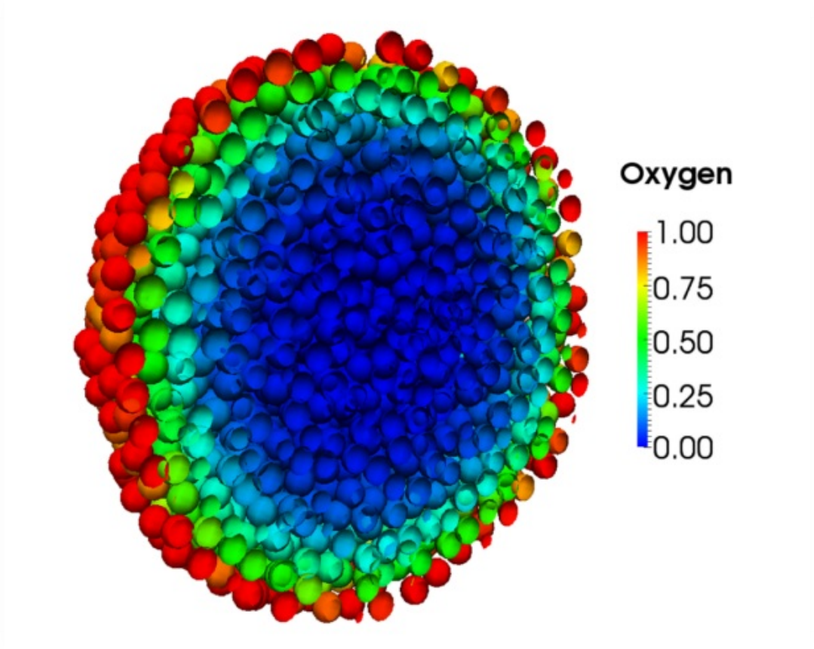
ABMs in cancer research

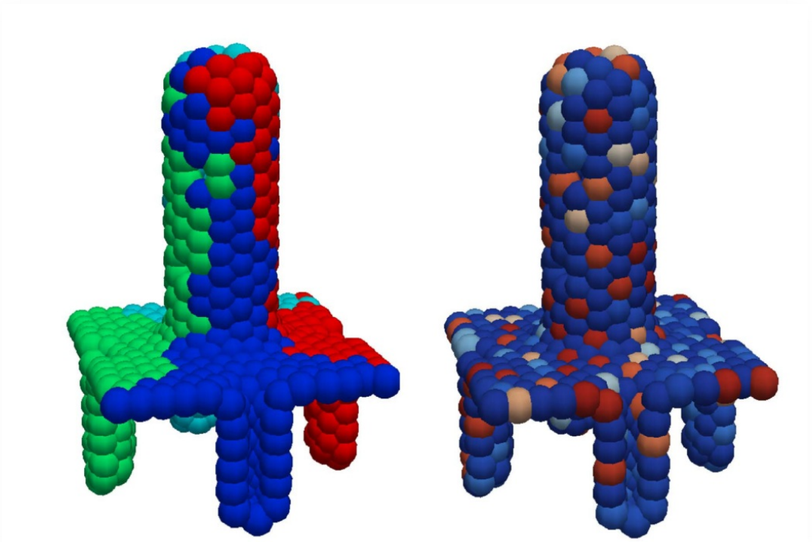
- Tumor growth
- Phenotypes
- Dynamics of mutation accumulation
- Mostly deterministic laws (PDE)

examples ABM in cancer

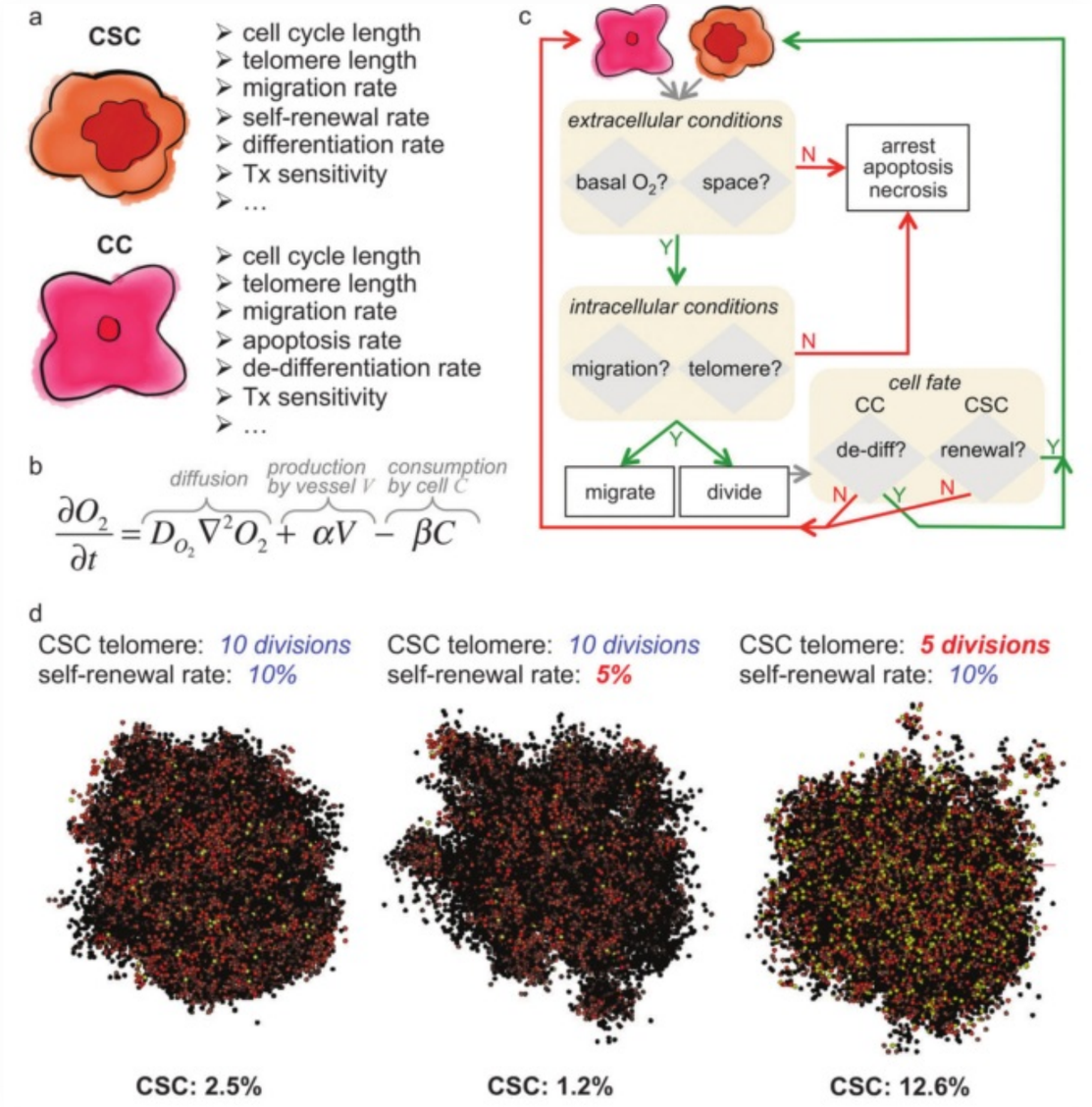


examples ABM in cancer





Enderling 2014 (CSC)



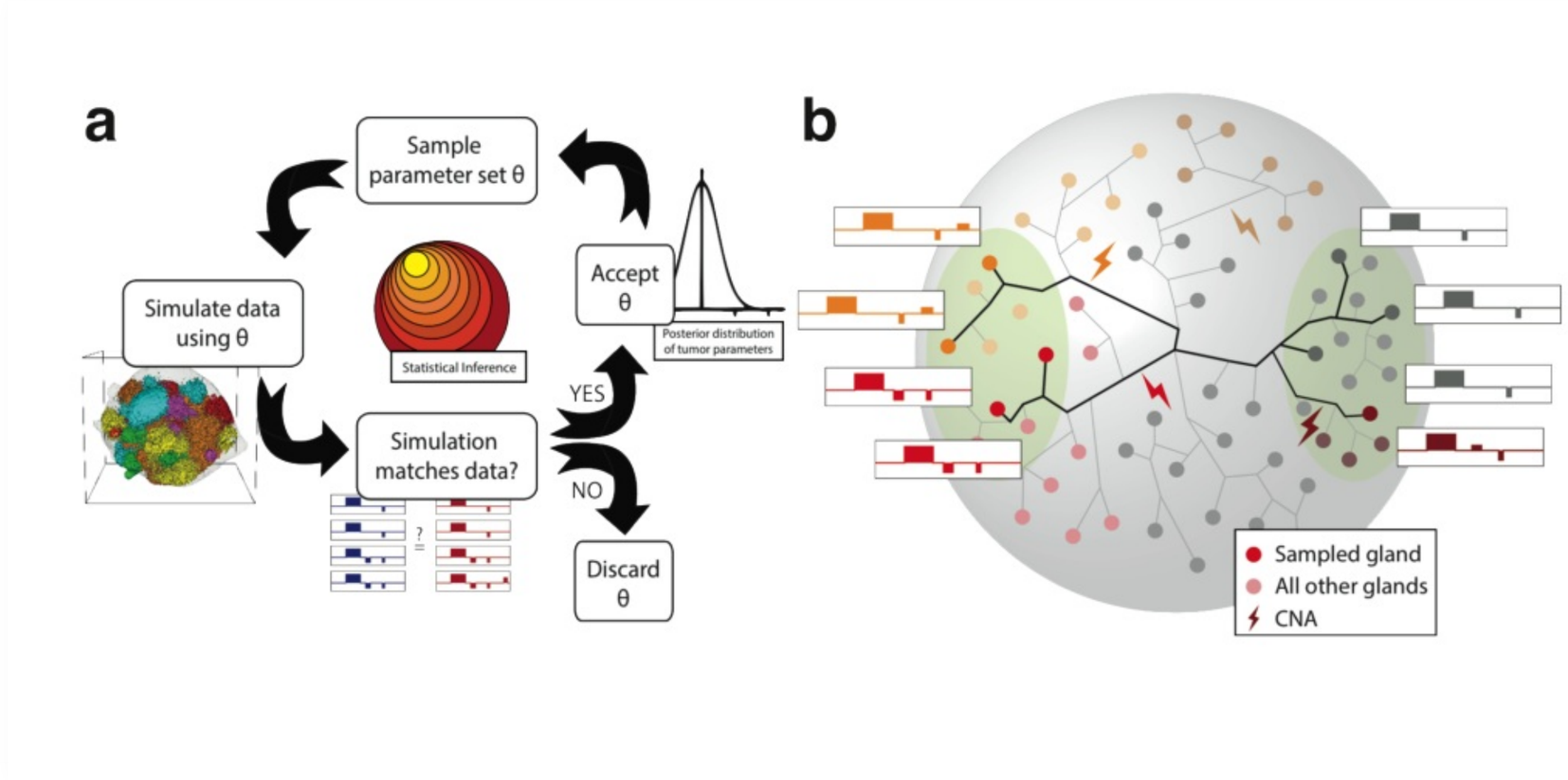
Sottoriva 2015 (Big Bang in CRC)

- Agents: Glands (8M -> 80 billion cells)
- Growth by fission (variable rates), occurrence of CNAs and mutations
- All cells in a gland same fitness (survival and growth)
- Parameters: mutation rate and fitness change
- Not modeled: cellular migration, apoptosis within a gland, the contribution of the surrounding normal tissue or angiogenic factors.

Sottoriva 2015 (Big Bang in CRC)

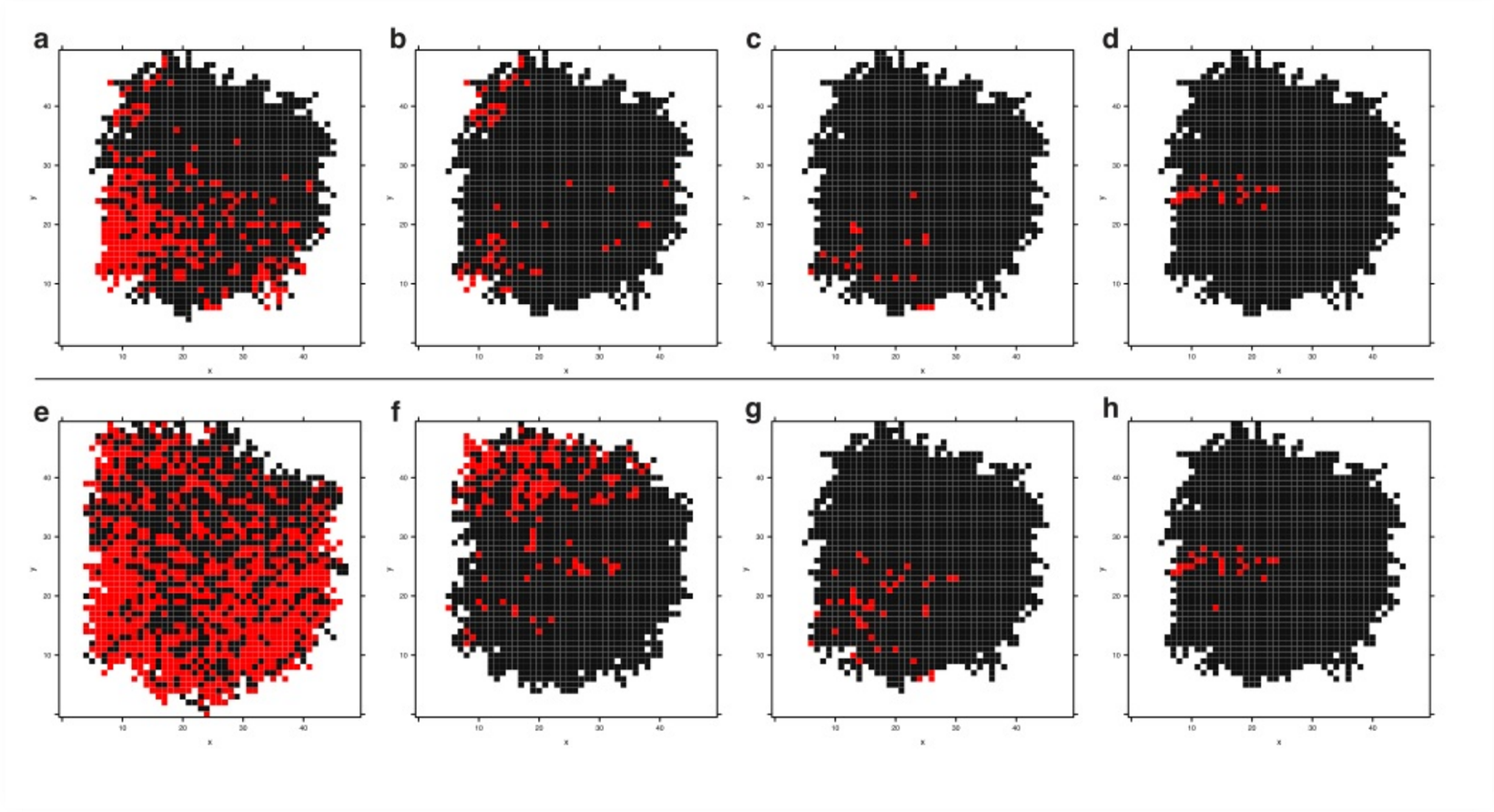
- 400x400x400 lattice
- Starting from a single gland until 80M reached
- Sampling regions
- ABC to fit observed data

Sottoriva 2015 (Big Bang in CRC)



Sottoriva 2015 (Big Bang in CRC)

- Neutral clone



Our interests

- Final goal is to do a general simulator of intratumoral pop gen.
- Start with a simple model, including selection and genealogy of all the alleles/clones
- Define and separate fitness traits (proliferation speed, growth speed, adhesion)
- Different set of genes/mutations for different traits (pleiotropy?)

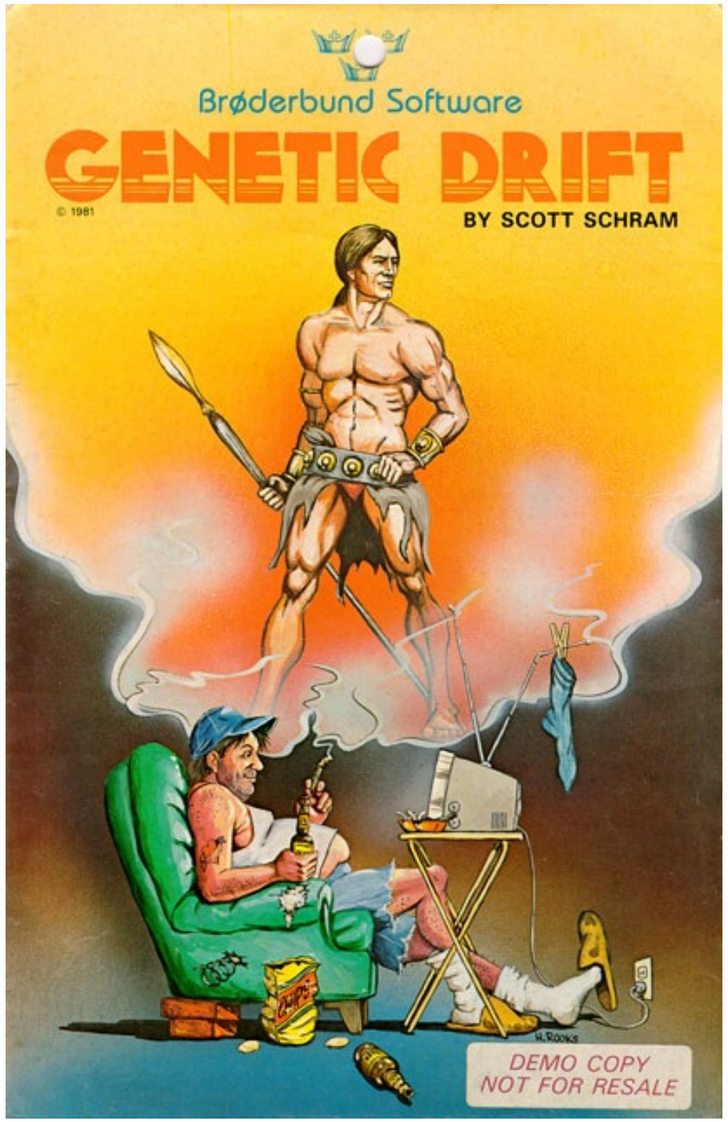
Limitations

- Huge computational cost of ABMs
- Limited number of agents or time units
- Reduced genome representation

Further readings

Follow this link for a list of references for this talk:
http://bit.ly/1TmtseB

Thanks for coming



Presentation made with reveal.js. Get source at:
https://github.com/anpefi/slides-seminar-IBMsims