FROM AN INDIVIDUAL-BASED MODEL TO PARTIAL DIFFERENTIAL EQUATIONS: AN APPLICATION TO THE STUDY OF YEAST POPULATIONS IN BATCH CULTURES

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Mathematical and Computational approaches provide powerful tools in the study of problems in population biology and ecosystems science.

The subject has a rich history intertwined with the development of statistics and dynamical systems theory, but recent analytical advances, coupled with the enhanced potential of high-speed computation, have opened up new vistas and presented new challenges.

Individual-based Models (IbM) or "agent-based" models

They are a bottom-up approach which starts with the 'parts' (individuals) of a system and then tries to understand how the system's properties emerge from the interaction among these 'parts'.

Four criteria that distinguish what we consider IbM
(1) The degree to which the complexity of the individual's life cycle is reflected in the model
(2) The extent to which variability among individuals of the same age, size or stage is considered
(3) Whether or not the spatial and temporal dynamics of resources used by individuals are explicitly represented
(4) Whether real or integer number are used to represent the size of a population (IbM are built using the mathematics of discrete events)

Advantages of IbM

- More realistic assumptions than state variable models.
- Individuals are described by attributes and capabilities: grow, develop, acquire resources, reproduce, interact, changing in many ways over their life cycle and modifying their environment.
- The simulations provide information on the collective behaviour by looking at the behaviour of each element of which it is composed.
- They can address types of questions difficult to be addressed with classical models.
- Highly detailed models with a wide variety of components and mechanisms.
- Controlled simulation experiments to achieve a comprehensive understanding of the key structures and processes.

Disadvantages of IbM

- The amount of detail is often too high to be supported in terms of what we can measure and parameterize.
- Extensive simulations constitute a brute-force method still lacking an analytical or theoretical framework.
- Mostly applied to pragmatic motivations rather than paradigmatic.
- More complex than classical and analytically tractable models: many entities, spatial scales, heterogeneities and stochastic events.
- Absence of a common and concise language for communicating.

Lagrangian, individual-based, descriptions make attractive cartoons and can provide a basis for population features analysis.
Eulerian, partial differential equation based, field descriptions capture the essence of population dynamics.
We are interested in bridging the gaps between both approaches.

INDISIM (INDividual DIScrete SIMulations), a model that stands on individual-based methodology to study microbial systems. INDISIM-YEAST, an adaptation from INDISIM to study yeast populations in batch cultures.

YEAST POPULATION MODEL

- The set of $N(t)$ yeast cells conforms the population, defined by

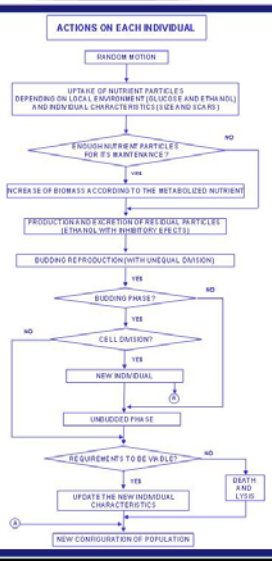
$$P(t) = \{Y_i(v_1(t), v_2(t), \ldots, v_{10}(t))\}_{i=1,2,\ldots N(t)}$$

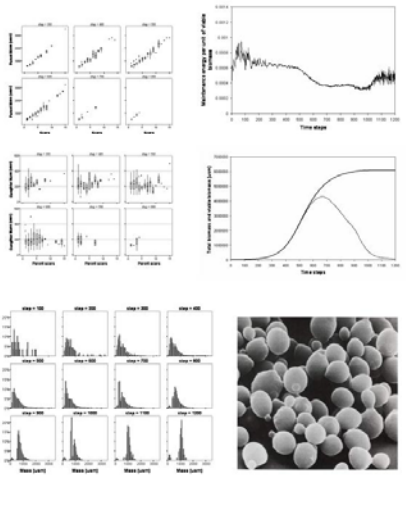
Y_i is a yeast cell with the following individual characteristics:
- v_1 : cell biomass
- v_2 : genealogical age as a number of bud scars on the cellular membrane
- (v_3, v_4, v_5) : position in the spatial domain
- v_6 : the reproduction phase in the cellular cycle, namely the unbudded or budding phase
- v_7 : "start mass", i.e., mass requiered to change from unbudded to budding phase
- v_8: minimum bud biomass to complete budding reproduction
- v_9: minimum time required to complete the budding phase
- v_{10}: survival time without satisfying the metabolic requirements

- The set of Q^3 spatial cubic cells configures the grid, defined by

$$G(t)=\{S_{ijz}[s_1(t), s_2(t)]\}_{i,j,z=1,\ldots Q}$$

S_{ijz} is a spatial cell, being $s_1(t)$ and $s_2(t)$ the number of glucose and ethanol particles respectively.





PARTIAL DIFFERENTIAL EQUATIONS for INDISIM-YEAST

Evolution equations

$$\frac{\partial \rho_1}{\partial t} = D_Y \triangle \rho_1 - \frac{\partial}{\partial m}(\rho_1 \eta) - \frac{\partial}{\partial m_I}(\rho_1 \eta) - \frac{\partial}{\partial t_s}(\rho_1 v_{st}) - d\rho_1 + \tau_{21}\rho_2 - \tau_{12}\rho_1$$

$$\frac{\partial \rho_2}{\partial t} = D_Y \triangle \rho_2 - \frac{\partial}{\partial m}(\alpha \rho_2 \eta) - \frac{\partial}{\partial m_B}((1-\alpha)\rho_2 \eta) - \frac{\partial}{\partial a}(\rho_2 v_{sc}) - \frac{\partial}{\partial a_B}(\rho_2) - \frac{\partial}{\partial t_s}(\rho_2 v_{st}) - d\rho_2 + \tau_{12}\rho_1 - \tau_{21}\rho_2$$

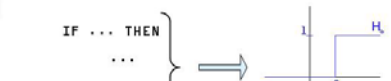
$$\frac{d\rho_g}{dt} = D_g \triangle \rho_g - U\rho_1 - U\rho_2$$

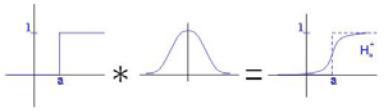
$$\frac{d\rho_e}{dt} = D_e \triangle \rho_e + \beta U \rho_1 + \beta U \rho_2$$

$\vec{x}$: position in the 3D domain Ω
t: time
m: yeast biomass
t_s: energy store, survival time without nutrient suply
m_I: mass increased since last bud
a: genealogical age
m_B: bud biomass
a_B: time since the start of bud formation

$\rho_1 = \rho_1(\vec{x}, t; m, t_s, m_I, a)$: density of cells in the unbudded phase
$\rho_2 = \rho_2(\vec{x}, t; m, t_s, m_B, a, a_B)$: density of cells in the budding phase
$\rho_g = \rho_g(\vec{x}, t)$: density of glucose
$\rho_e = \rho_e(\vec{x}, t)$: density of ethanol

IF ... THEN
...
...
ENDIF





Boundary conditions

$$\rho_1(\vec{x}, t; m, t_s, m_I = 0, a) = \int \tau_{21}\rho_2$$

$$\rho_2(\vec{x}, t; m, t_s, m_B = 0, a, a_B = 0) = \int \tau_{12}\rho_1$$

$$\rho_1(\vec{x}, t; m = m_B, t_s, m_I = 0, a = 0) = \int \tau_{21}\rho_2$$

$$\tau_{12}(m, m_I) = H^*_{M_c}(m)\, H^*_{M_{cI}}(m_I)$$

$$\tau_{21}(m_B, a_B) = H^*_{M_B}(m_B)\, H^*_{A_B}(a_B)$$

Initial conditions

$$\rho_1(\vec{x}, t=0; m, m_s, m_I, a) = \rho_{1o}(\vec{x})$$
$$\rho_2(\vec{x}, t=0; m, m_s, m_B, a, a_g) = 0$$
$$\rho_g(\vec{x}, t=0) = \rho_{go}(\vec{x})$$
$$\rho_e(\vec{x}, t=0) = 0$$

The bridge between the IBM and the PDEs is obtained by considering a moderately interacting particle system which includes all the "parts" of the system; the number of particles is assumed to grow to infinity, yielding a weak form of the PDE system.

The processes taking place continually (such as transport and Brownian motion) are dealt with by a set of stochastic differential equations.

The point processes which induce discontinuous changes in the population (such as cellular division, death and cell phase transitions) are mathematically described as nonconstant-intensity Poisson processes.

Future work:

- Numerical resolution of the PDE system.

- Comparison of this solution with the IbM realizations.

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*Picture courtesy of Verema, http://www.verema.com/opinamos/tribuna/articulos/levaduras02.htm

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