International Day of Women and Girls in Science

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Mathematical models for oncology: a synergy of sciences towards personalised medicine

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XXXVI cycle (PoliTO - UniTO)
Models and Methods in Mathematical Physics

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Summary

1. WHAT
   - Integrated mathematical oncology
   - Mathematical modeling
2. HOW
   - Our choices
   - Our model
   - Our results
   - Therapies
3. WHY
   - Classifying tumors
   - Personalized medicine
4. WHO

WHAT: Integrated mathematical oncology

Oncology

Prevention, diagnosis, and treatment of cancer

Biomathematics

Describing biological processes and their relations in mathematical terms

System biology

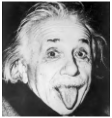
Understanding complex systems by putting pieces together

Mathematical modeling

- Cellular dynamics
- Interaction with the environment
- Epigenetic

WHAT: Mathematical modeling

Biological information
↓
First model
↓
Refined model
↓
Prediction



Everything should be made as simple as possible.
But not simpler.

WHAT: Mathematical modeling

Choice of:

- space and/or time scale(s)
- approach (continuous, discrete, hybrid)
- mathematical formulation

Biological information

↓

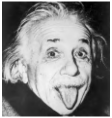
First model

↓

Refined model

↓

Prediction



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WHAT: Mathematical modeling

Aims:

- adherence:
  - quality of data fit
  - coherence with scientific knowledge
- simplicity:
  - theoretical predictability
  - numerical solvability
  - lower computational cost

Biological information

↓

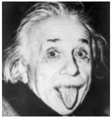
First model

↓

Refined model

↓

Prediction



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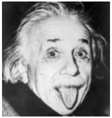
WHAT: Mathematical modeling

IN SILICO EXPERIMENTS

- WHERE: on the machine, outside the patient body
- WHEN: before processes happen

Biological information → First model → Refined model → Prediction



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HOW: Our Choices

- Continuous approach
- Meso/macro scale: cell dynamics, population point of view
- Interactions: oxygen (respiration, survival), lactate (survival)
- 3d space: phenotypic space and geometric space

G. Fiandaca, M. Delitala, T. Lorenzi, A mathematical study of the influence of hypoxia and acidity on the evolutionary dynamics of cancer cells in vascularised tumours

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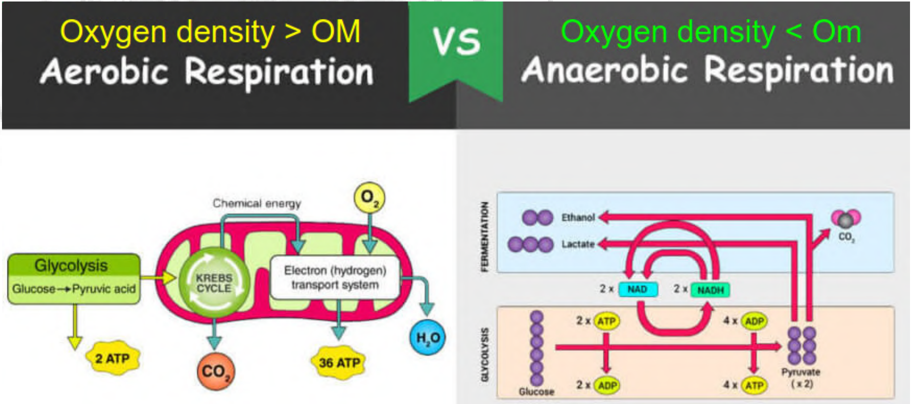

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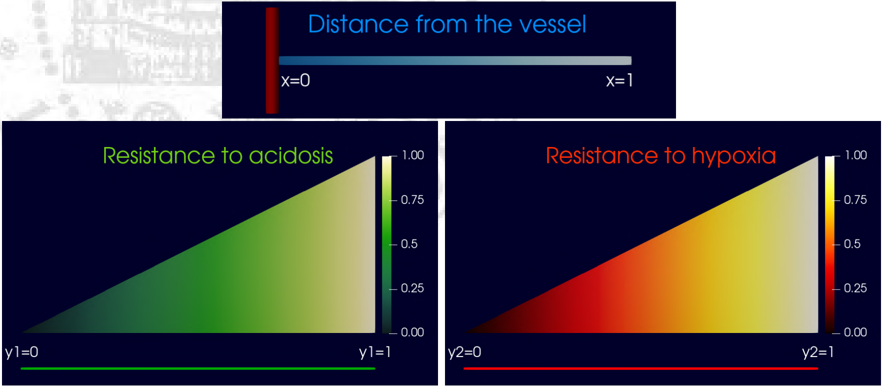

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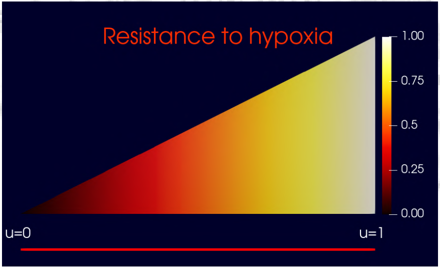

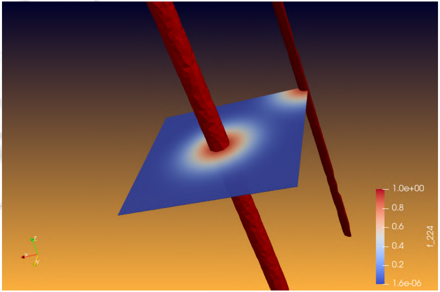

HOW: Our Model (1 spacial, 2 phenotypic)

$$
\begin{aligned}
\frac{\partial n}{\partial t} &= \beta_n \frac{\partial^2 n}{\partial x^2} + \theta \left(\frac{\partial^2 n}{\partial {y_1}^2} + \frac{\partial^2 n}{\partial {y_2}^2} \right) + R(O, L, \rho, \mathbf{y})\, n \\
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\end{aligned}
$$

Functions

- $n(t, x, y_1, y_2)$ = cancer cell density
- $O(t, x)$ = oxygen density
- $L(t, x)$ = lactate density

HOW: Our Model (1 spacial, 2 phenotypic)

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Elements

Oxygen/Lactate density

- Diffusion
- Decay
- Consumption/production by cancer cells

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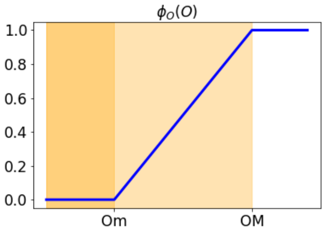
Consumption

$$p_O(O) = \frac{\gamma_O O}{\alpha_O + O}\, \phi_O(O)$$

Spacial Distribution

$$\rho(t, x) = \int_0^1 \int_0^1 n(t, x, y_1, y_2) dy_1 dy_2$$



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Production

$$p_G(O) = \frac{\gamma_G G}{\alpha_G + G} (1 - \phi_O(O))$$

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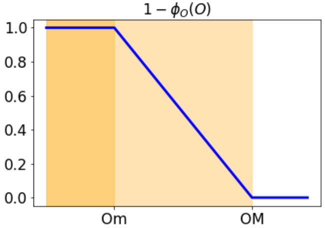

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Cancer cells density

- Diffusion
- Random mutation
- Fitness

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$$R(O, L, \rho, \mathbf{y}) = p_O(O) - S(O, L, \mathbf{y}) - D(\rho)$$

Fitness

Cancer cells density

- Proliferation
- Selection
- Death

HOW: Our Model (1 spacial, 2 phenotypic)

$$\frac{\partial n}{\partial t} = \beta_n \frac{\partial^2 n}{\partial x^2} + \theta\left(\frac{\partial^2 n}{\partial {y_1}^2} + \frac{\partial^2 n}{\partial {y_2}^2}\right) + R(O, L, \rho, \mathbf{y})\, n$$

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Cancer cells density

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- Death

Death

Space-competition-induced death

$D(\rho) = \kappa\rho$

HOW: Our Model (1 spacial, 2 phenotypic)

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Fitness

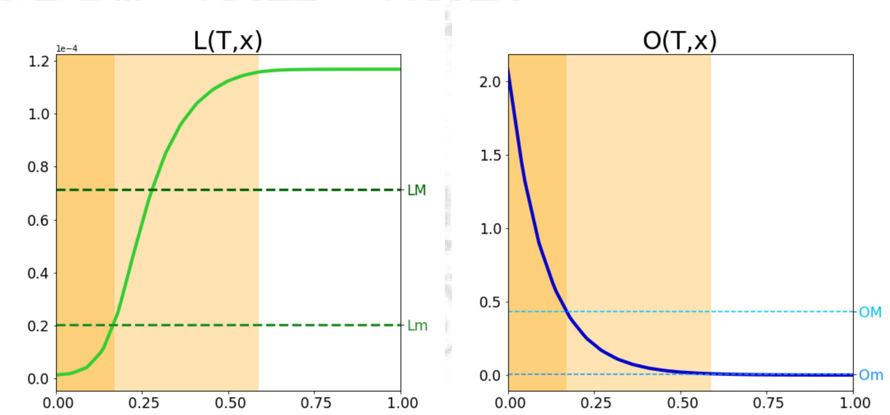
Cancer cells density

- Proliferation
- Selection
- Death

Selection

- Oxygen-driven:
  $S_L(L, y_1) = \eta_L \left(y_1 - \phi_L(L)\right)^2$
- Lactate-driven:
  $S_O(O, y_2) = \eta_O \left(y_2 - \phi_O(O)\right)^2$

HOW: Our results



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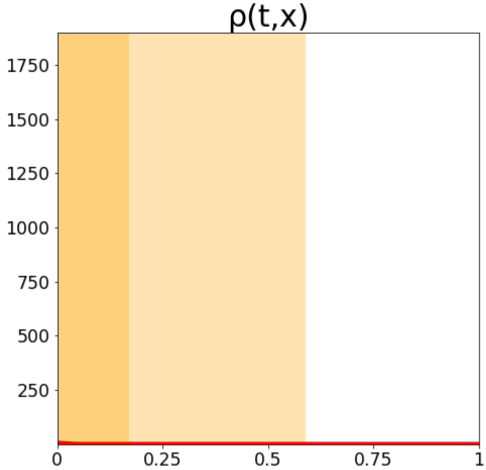

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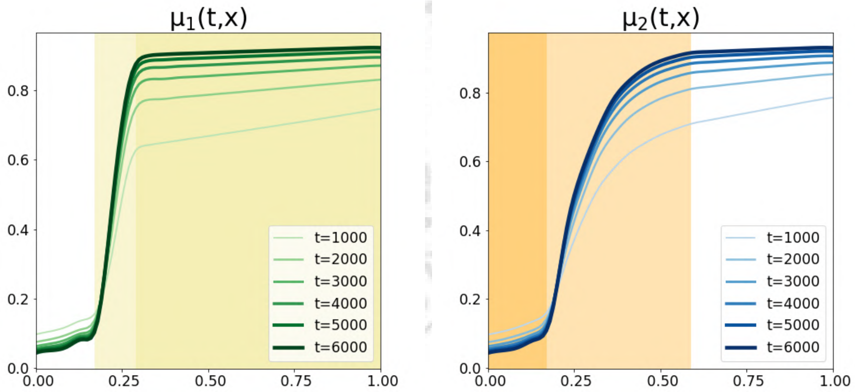
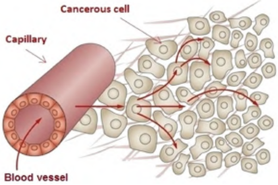


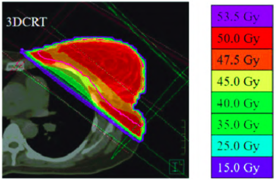
HOW: Therapies (next step)

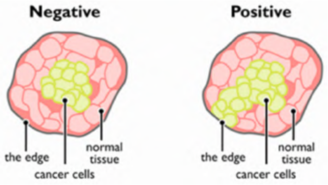
- Chemotherapy
- Radiotherapy
- Surgery

The structure of the models allows to keep into account:

- geometry of the therapy
- effect on therapy efficacy of the resistance to hypoxia/acidosis
- effect of therapy on remaining cells (if any)



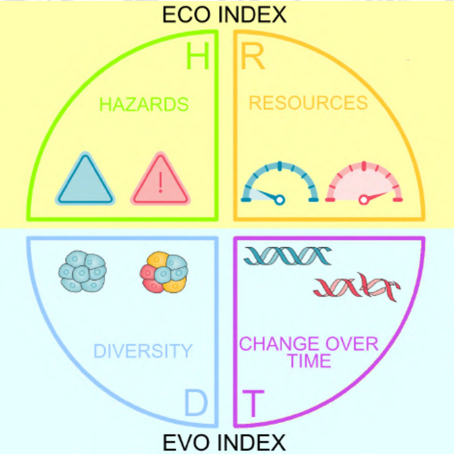


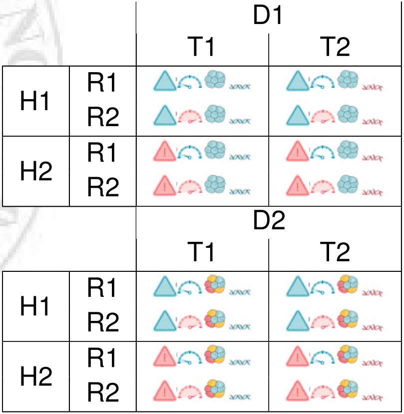


H. Namazi et al., Scientific Reports volume 5 (2015)
A. Nagai et al., Journal of Radiation Research (2017)
https://orchid-cancer.org.uk/

WHY: Classifying Tumors

PARTIAL AIM: classifying cancers in macro areas (eco-evo index)





C. Maley et al., Classifying the evolutionary and ecological features of neoplasms, Nature (2017)

WHY: Personalized medicine

FINAL AIM: individual protocols

Predictive model

↓

Insertion of patient data

↓

Simulation of tumor outcome

↓

Individuation of the macro area (first protocol selection)

↓

Simulation of different protocols on patient specific tumor

↓

Choice of the best therapy

BIGGER

=

STRONGER

=

BETTER

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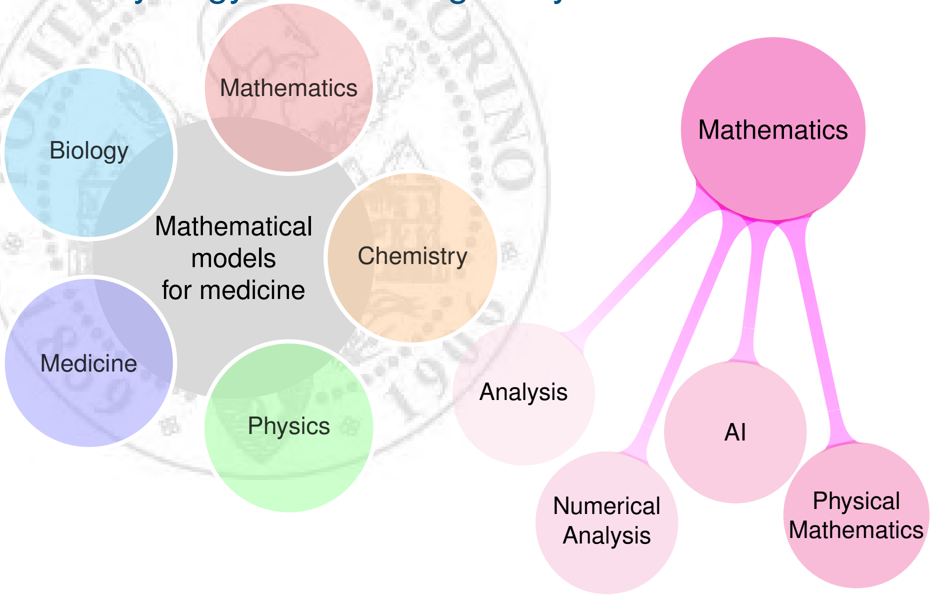
~~BIGGER~~
~~=~~
~~STRONGER~~
~~=~~
~~BETTER~~

WHO: Synergy and Heterogeneity



Thank you for your attention