A Scale Separation Approach Applied to a Mathematical Model of Solid Tumour Growth

Barbara de Melo Quintela,

Silvia Hervas-Raluy,

Jose Manuel Garcia-Aznar,

Dawn Walker,

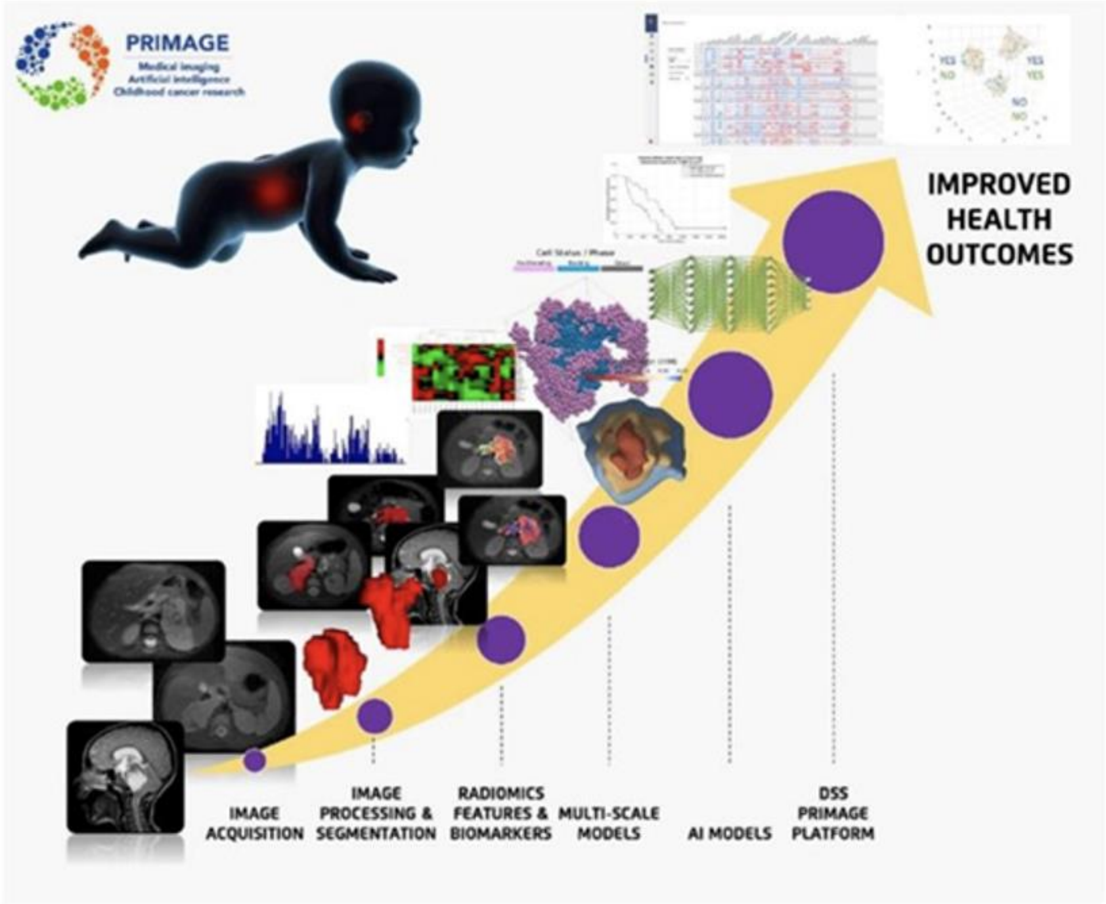
Kenneth Y Wertheim,

Marco Viceconti

PRIMAGE Project

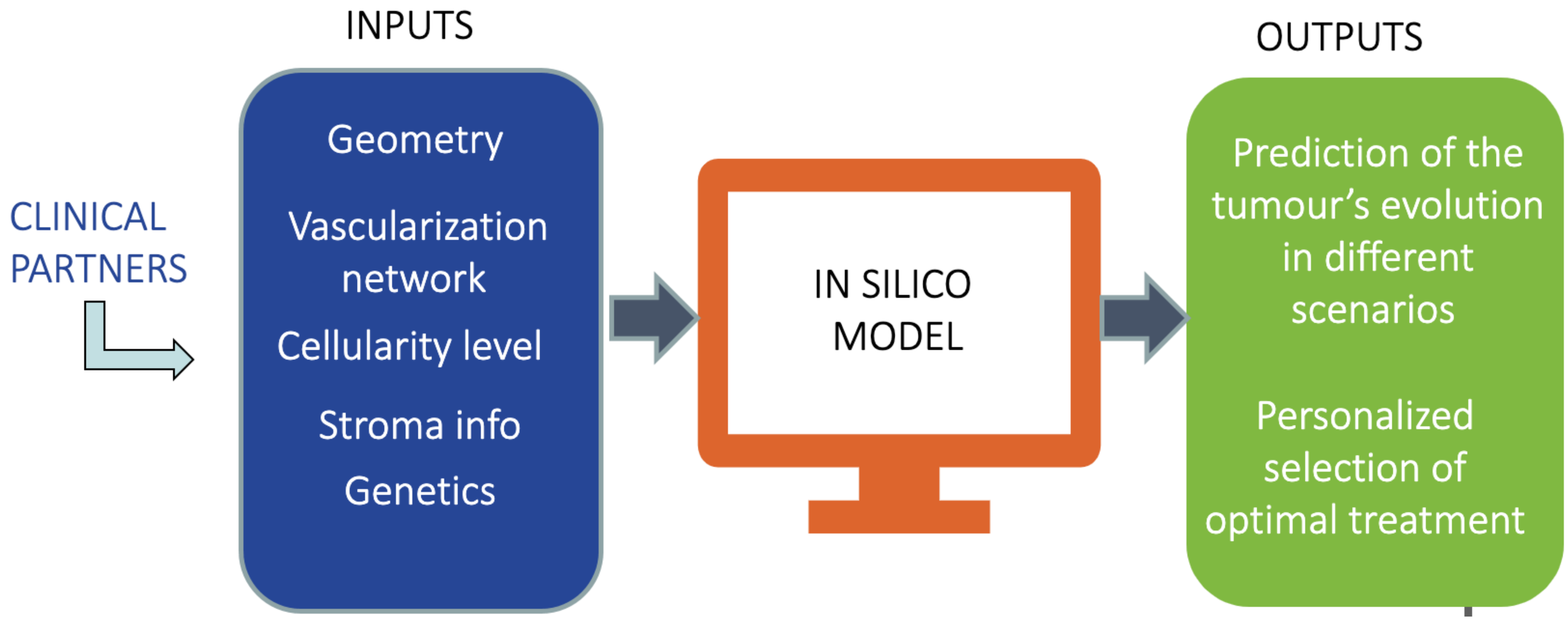
- **PR**edictive **I**n silico **M**ultiscale **A**nalytics to support cancer personalized dia**G**nosis and prognosis, **E**mpowered by imaging biomarkers

- Patient specific models of the tumour growth to personalize treatment
  - Neuroblastoma (NB) - Most frequent solid tumour outside of the brain in children

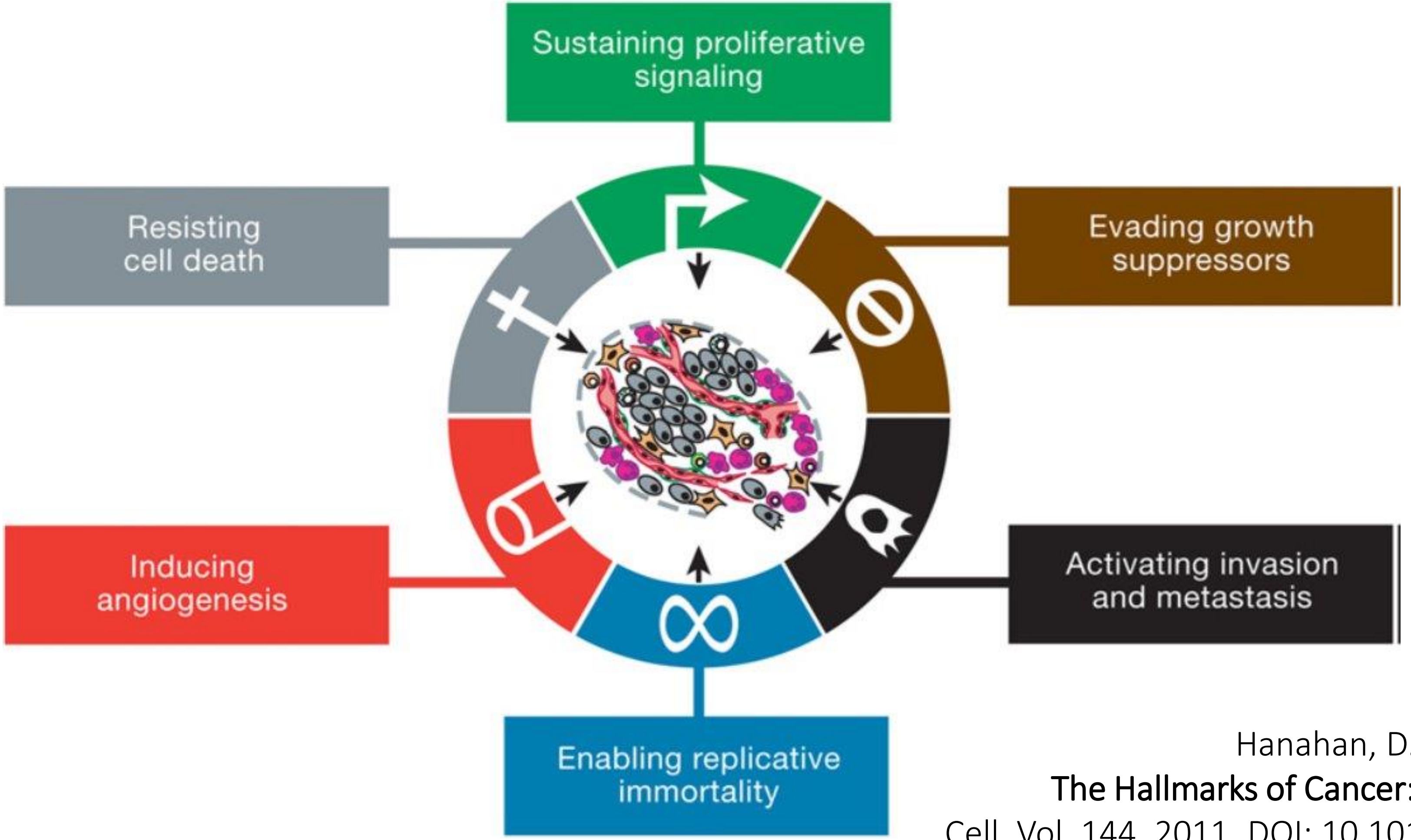


(Martí-Bonmatí *et al*. 2020)

Continuous Model - Tumour growth and chemotherapy outcome



Motivation



Hanahan, D. and Weinberg, R. A.
The Hallmarks of Cancer: the next generation.
Cell. Vol. 144, 2011. DOI: 10.1016/j.cell.2011.02.013

Question

How to separate the scales?

Definition of scale

- **Grain** - which is the largest value between the lower limit of spatial/temporal resolution allowed by instrumentation, and the smallest/fastest feature of interest.

- **Extent** - the smallest value between the upper limit of spatial/temporal resolution and the size of the largest/slowest feature to be observed.

Single Scale Infinite Resolution Mathematical Model

$$
\begin{cases}
\boldsymbol{\pi^*_{\gamma_k}(k(X), T_l, t) = \pi_{\gamma_k}\big(I_k, \alpha_k, \tau_k, S_1, \dots, S_J, t\big) \cdot \pi^{treat}_{\gamma_k}(T_l)} \\
r_i^{dV_X}(X,t) = \dfrac{dc_i^{dV_x}\big(X, S_1, \dots, S_J, t\big)}{dt} \\
\dot{S}_j(X,t) = \displaystyle\sum_k^{N \in dV_X} \chi_k^j(I_k, \alpha_k, \gamma_k, \tau_k, t) + \sum_k^{N \in dV_X} \sigma_k^j(I_k, \alpha_k, \gamma_k, \tau_k, t) \\
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\qquad (1)
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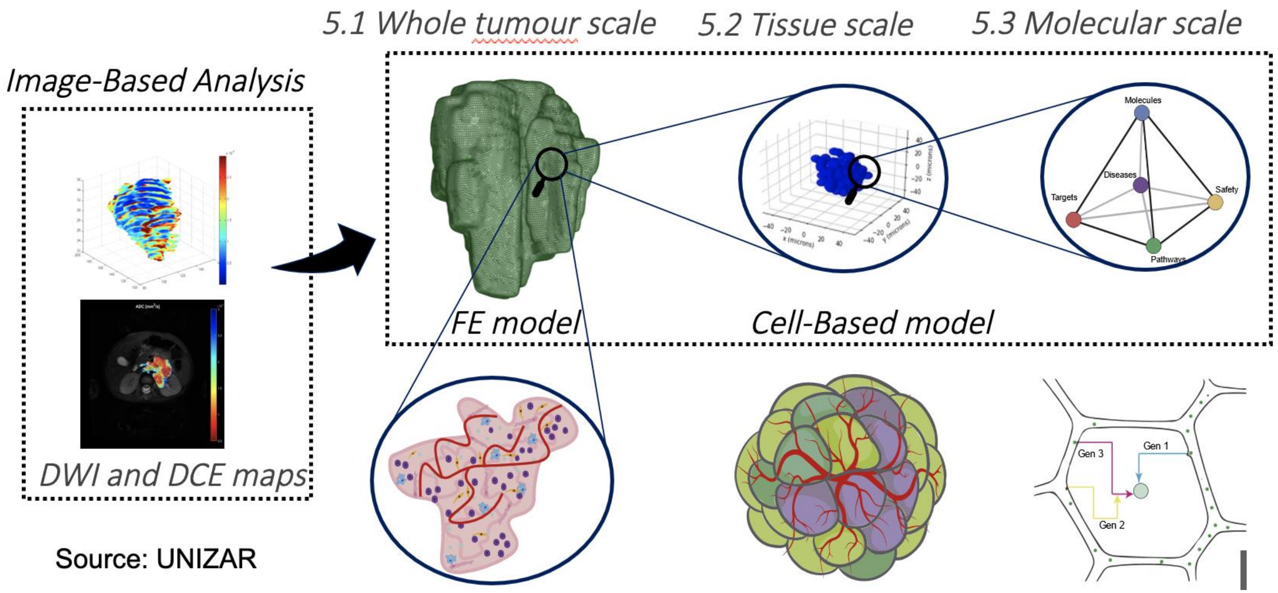
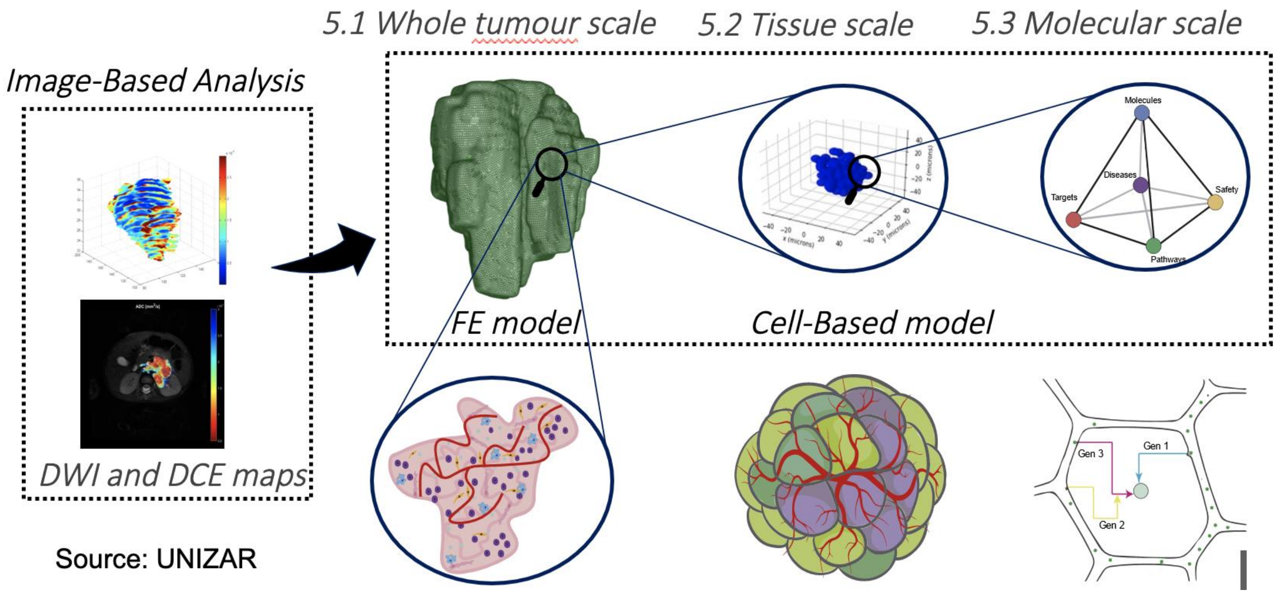
Multiscale Framework



Source: UNIZAR

- **Tumour**
  - Finite Element Method
- **Tissue**
  - Agent-Based Model
- **Cell**
  - Machine learning

Multiscale Framework



Source: UNIZAR

Temporal extent -> duration of chemotherapy

Temporal Grain -> minimum distance to successive imaging controls

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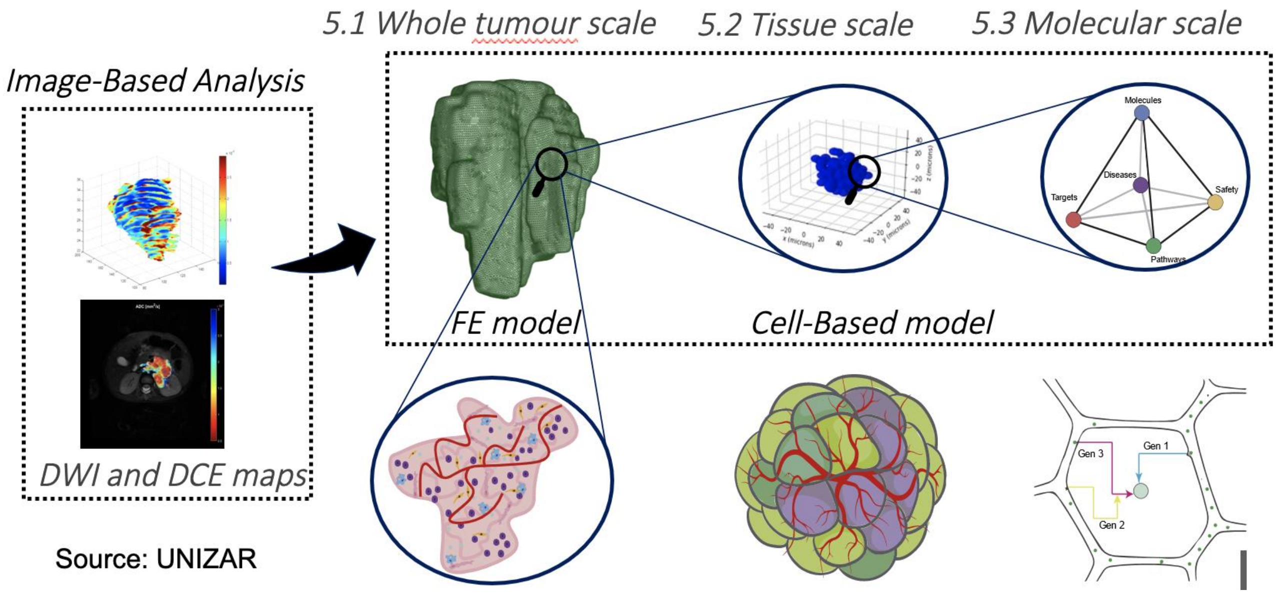
Multiscale Framework



Source: UNIZAR

Spatial extent -> size of tumour

Spatial Grain -> limited by image resolution and number of degrees of freedom the FEM can solve

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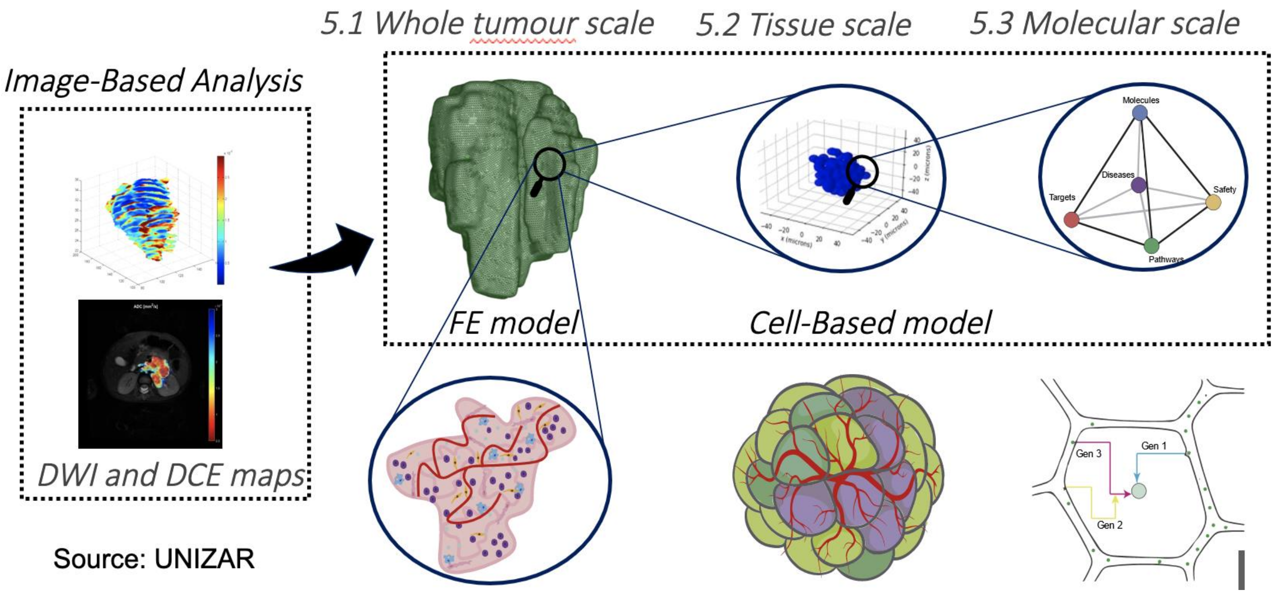

Source: UNIZAR

Spatial extent -> conveniently set to grain of tumour model
A tumour model with 300000 Finite Elements requires
300000 executions of the ABM

- **Tumour**
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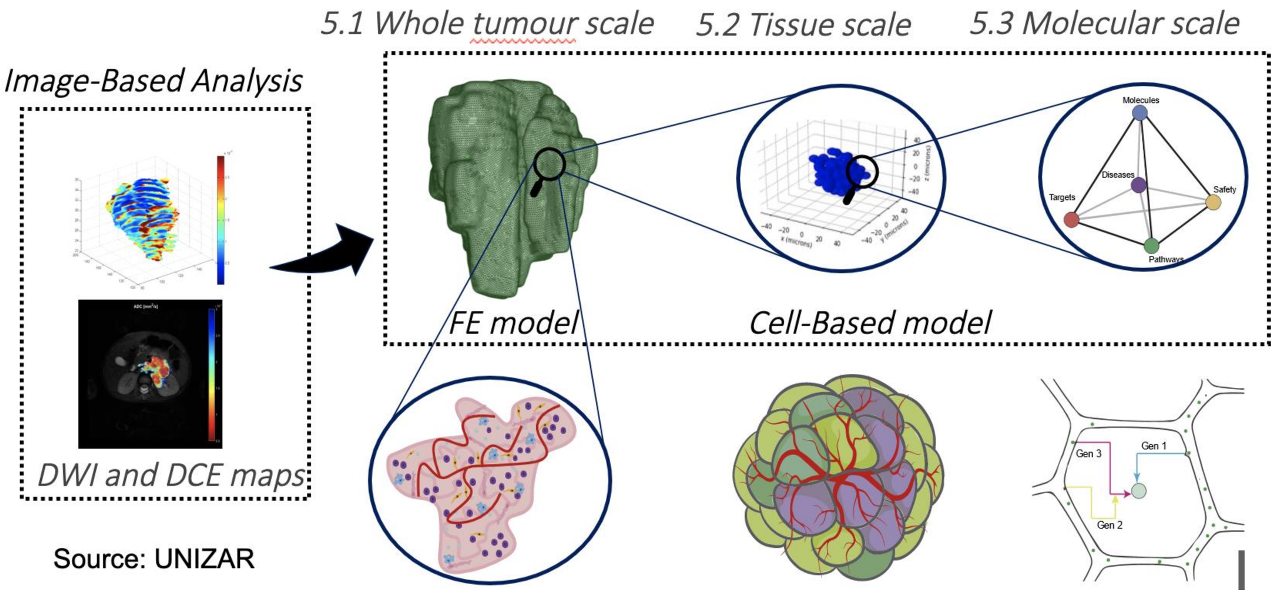


Source: UNIZAR

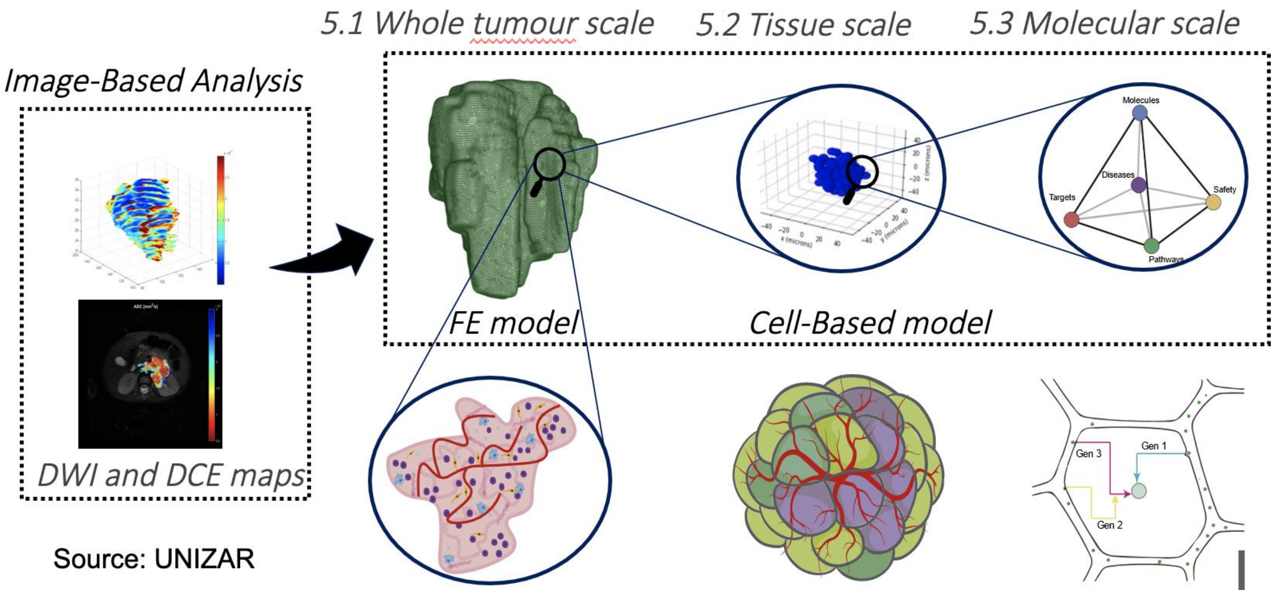
Spatial extent -> conveniently set to grain of tumour model
A tumour model with 300000 Finite Elements
requires 300000 executions of the ABM
- available HPC resources include 100 GPUs simultaneously

- **Tumour**
  - Finite Element Method

Binning ↓
Interpolation ↑

- **Tissue**
  - Agent-Based Model
- **Cell**
  - Machine learning

Multiscale Framework



Source: UNIZAR

Spatial and temporal extent of cell model -> conveniently set to grain of tissue model

- **Tumour**
  - Finite Element Method

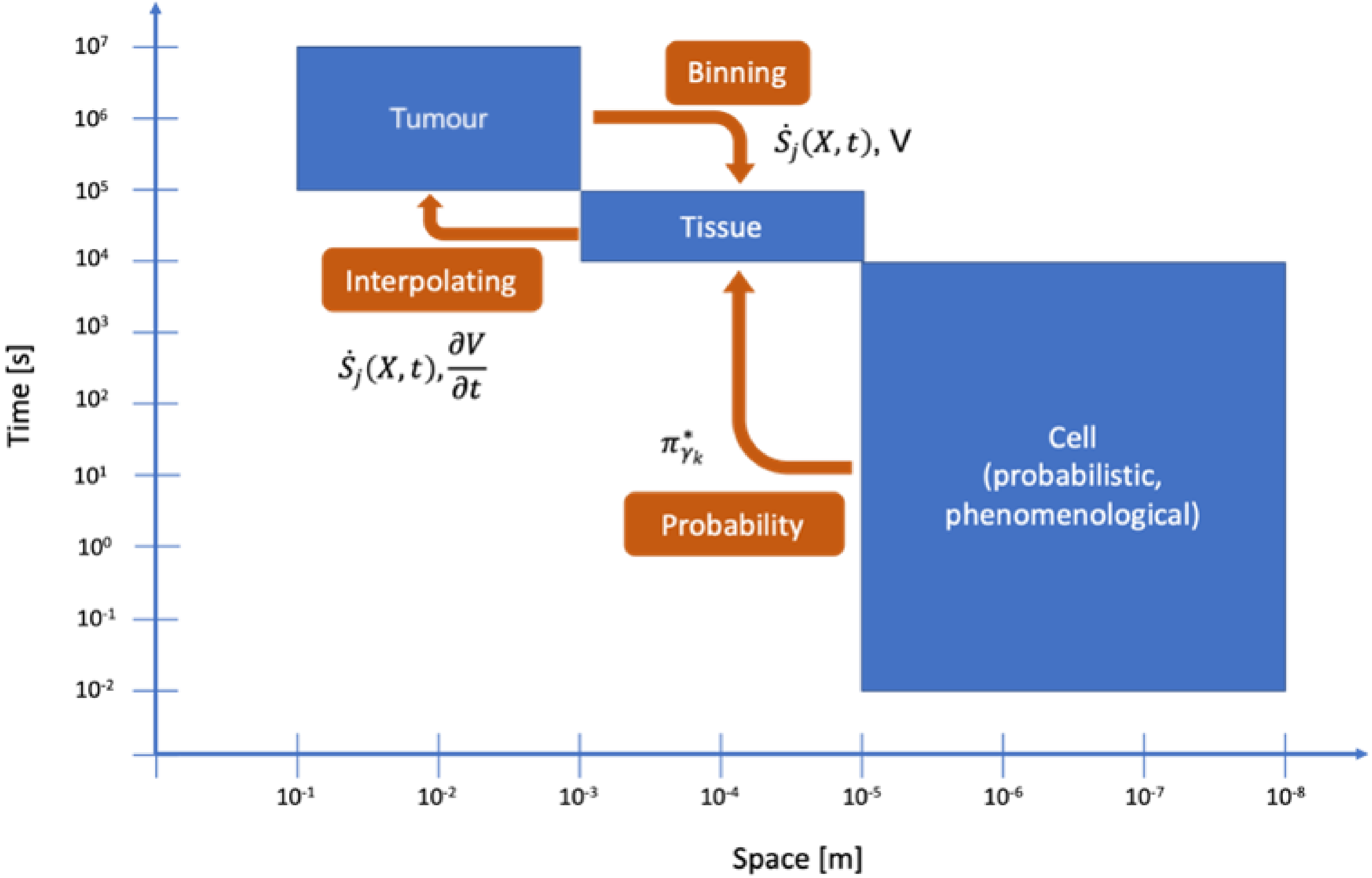
Binning ↓
Interpolation ↑

- **Tissue**
  - Agent-Based Model

↑ Not coupled, run once

- **Cell**
  - Machine learning

Scale separation applied to solid tumour growth



Considerations

- The aim of this study was to find the scale separation of a new multiscale tumour growth model that minimises the modelling complexity, while respecting the experimental resolution and computational constraints that limit the scale ranges.
- Reduction of hundreds of thousands of FE to a hundred ABM is a major simplification.
- Every paper that describes a multiscale model should provide justification for its scale separation based on the resolution of the experimental methods available to inform the model and the computational power available for its solution.

Thanks!

Barbara de Melo Quintela
Department of Computer Science, Federal University of Juiz de Fora, Juiz de Fora, Brazil.
barbara@ice.ufjf.br

Silvia Hervas-Raluy, Jose Manuel Garcia-Aznar
Multiscale in Mechanical and Biological Engineering (M2BE), Mechanical Engineering Dept, University of Zaragoza, Zaragoza, Spain.

Kenneth Y Wertheim, Dawn Walker
Department of Computer Science and Insigneo Institute of In Silico Medicine, University of Sheffield, Sheffield, UK.

Marco Viceconti
Department of Industrial Engineering, Alma Mater Studiorum - University of Bologna and Medical Technology Lab, IRCCS Istituto Ortopedico Rizzoli, Bologna, Italy.