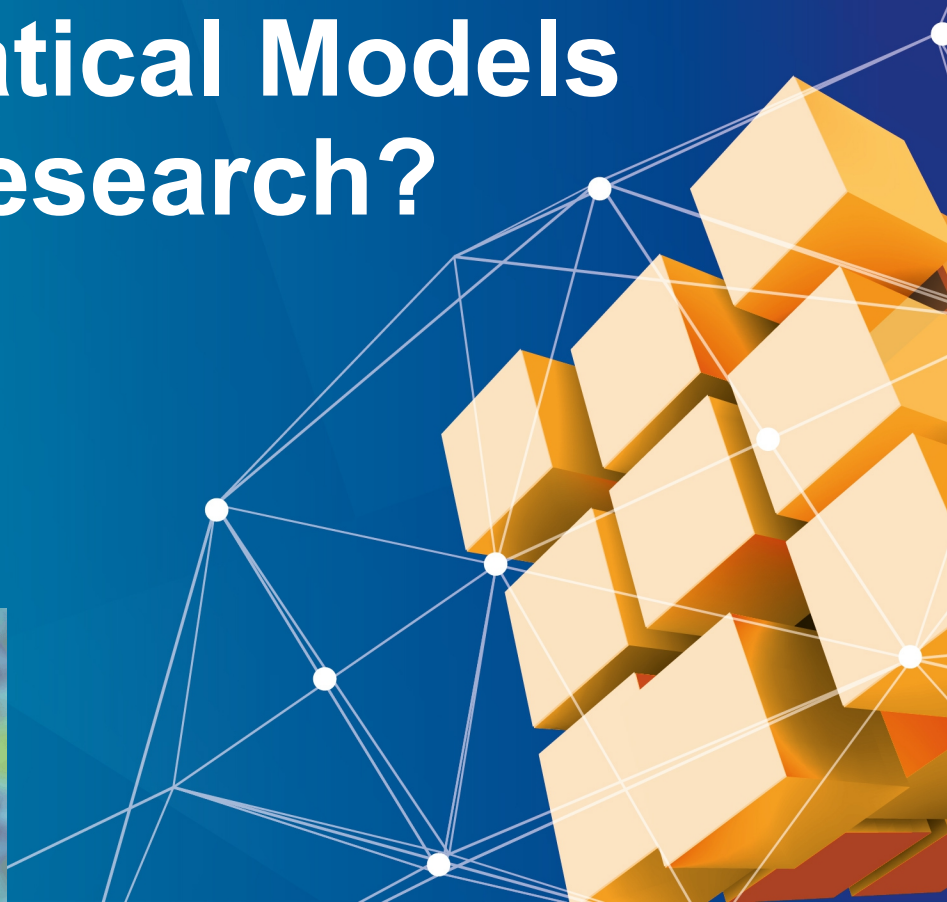
DISMA Dipartimento di Scienze Matematiche G. L. Lagrange

ECCELLENZA 2018 • 2022

How Can Mathematical Models Support Cancer Research?

Luigi Preziosi



POLITECNICO DI TORINO

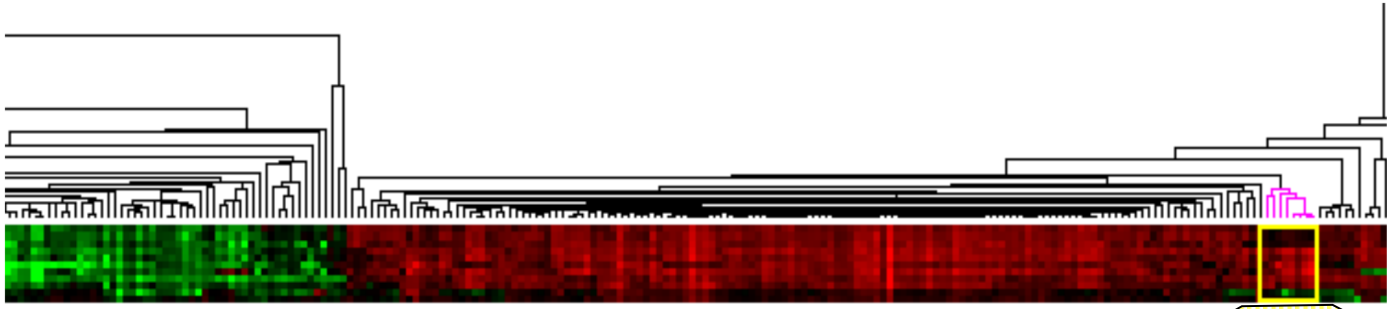
CIMAB

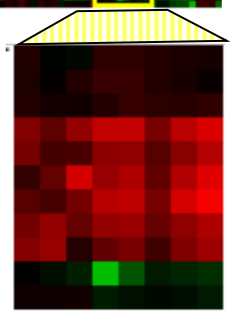
POLITECNICO DI TORINO

The hystorical moment

Decoding the genome

Genomic data

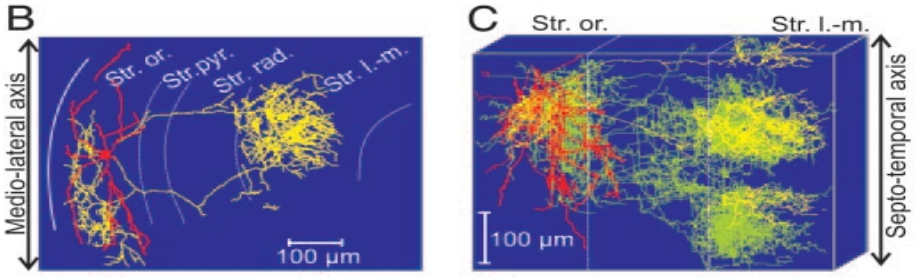




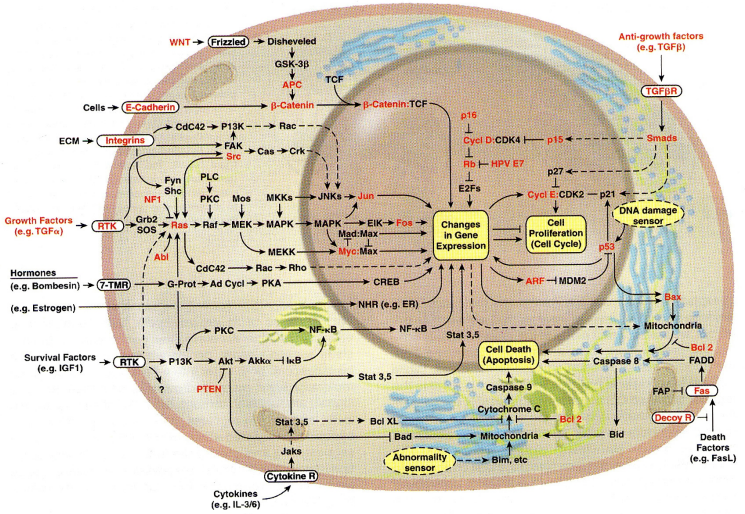
cyclin-dependent kinase in
Cyclin-dependent kinase in
retinoid X receptor, beta
CDK inhibitor p19INK4d mRN
CYCLIN-DEPENDENT KINASE IN
CYCLIN-DEPENDENT KINASE IN
Pim3 (PIG3) mRNA, complete
Damage-specific DNA bindin

- Organizing a huge quantity of data
- Extracting information

The same for other omics



connectomics



proteomics

POLITECNICO DI TORINO

The hystorical moment

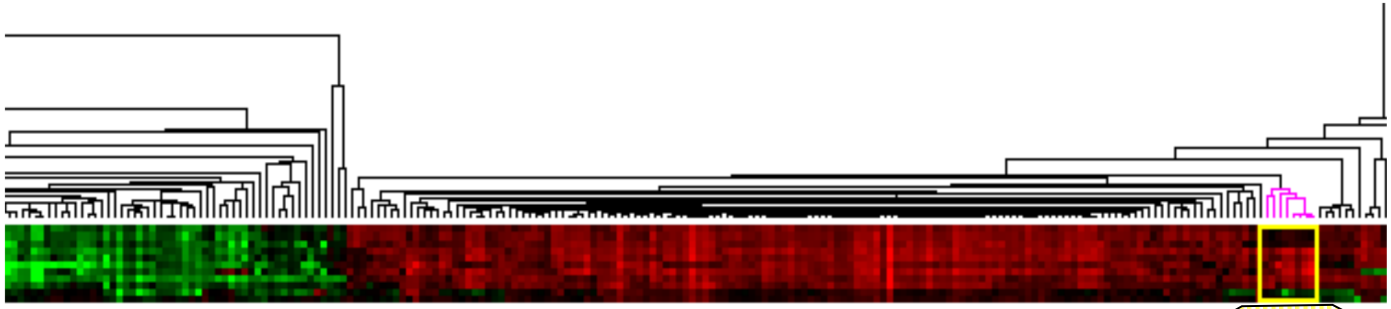
Decoding the genome

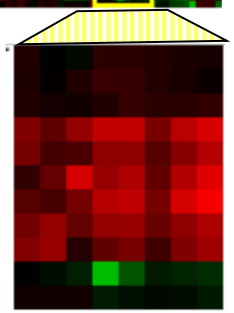
↓

Genomic data

↓

Organizing a huge quantity of data





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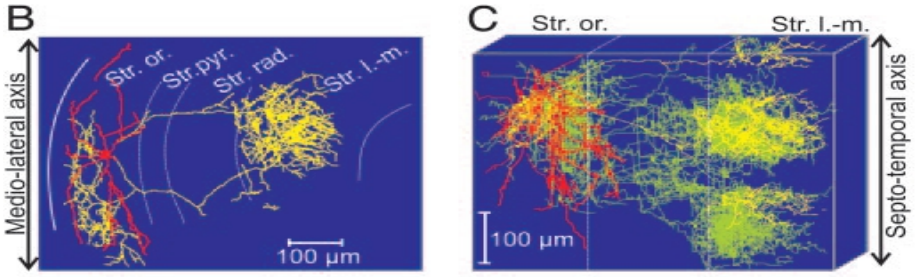
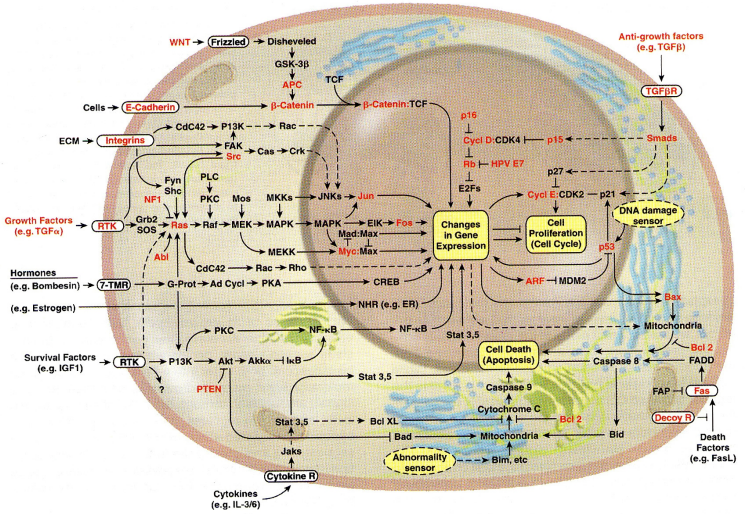


connectomics



proteomics

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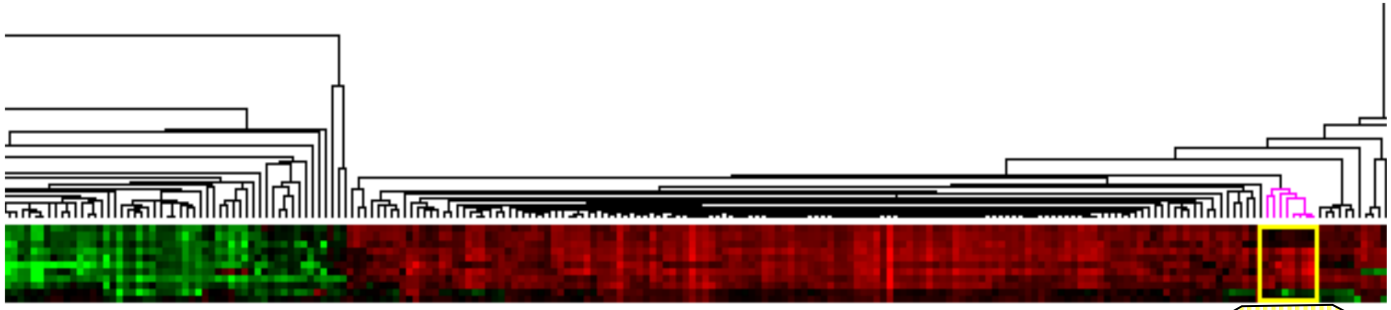
Type of problems

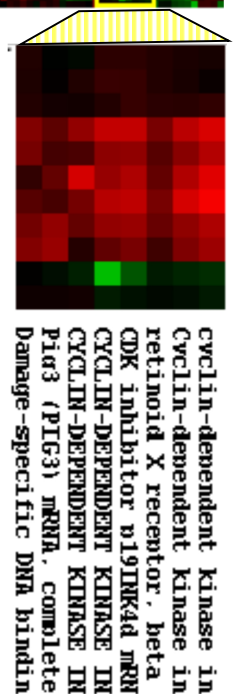
Decoding the genome

↓

Genomic data

↓



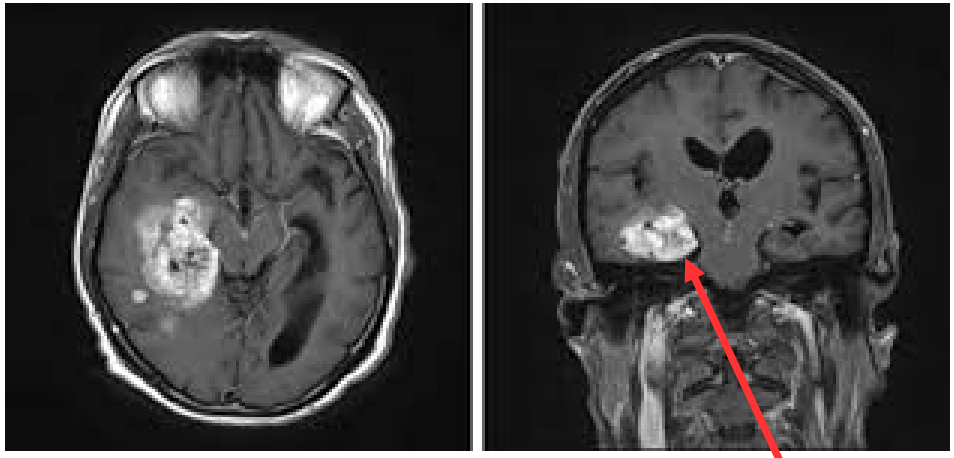


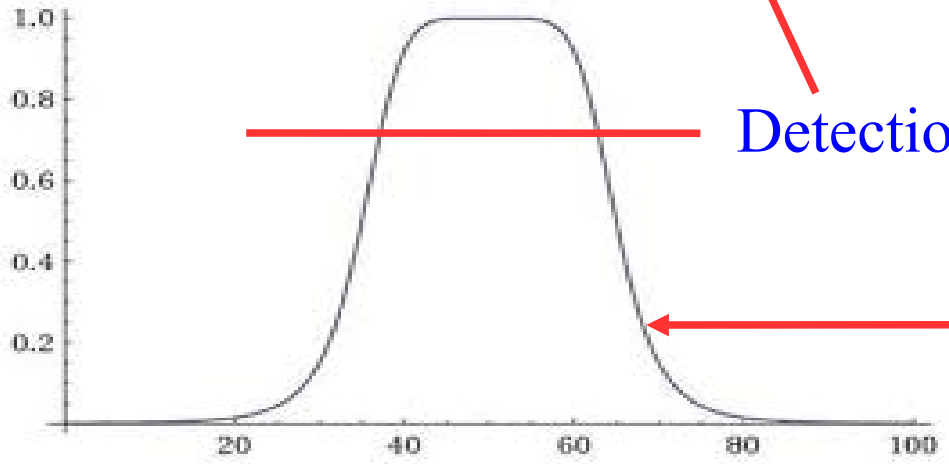
- Organizing a huge quantity of data — Statistical problems
- Understanding the past
- Imaging

} Inverse problems

- Foreseeing the future — Direct problems
- Optimizing & personalizing therapies — Control & optimization problems

Inverse problems





Detection threshold

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c$$

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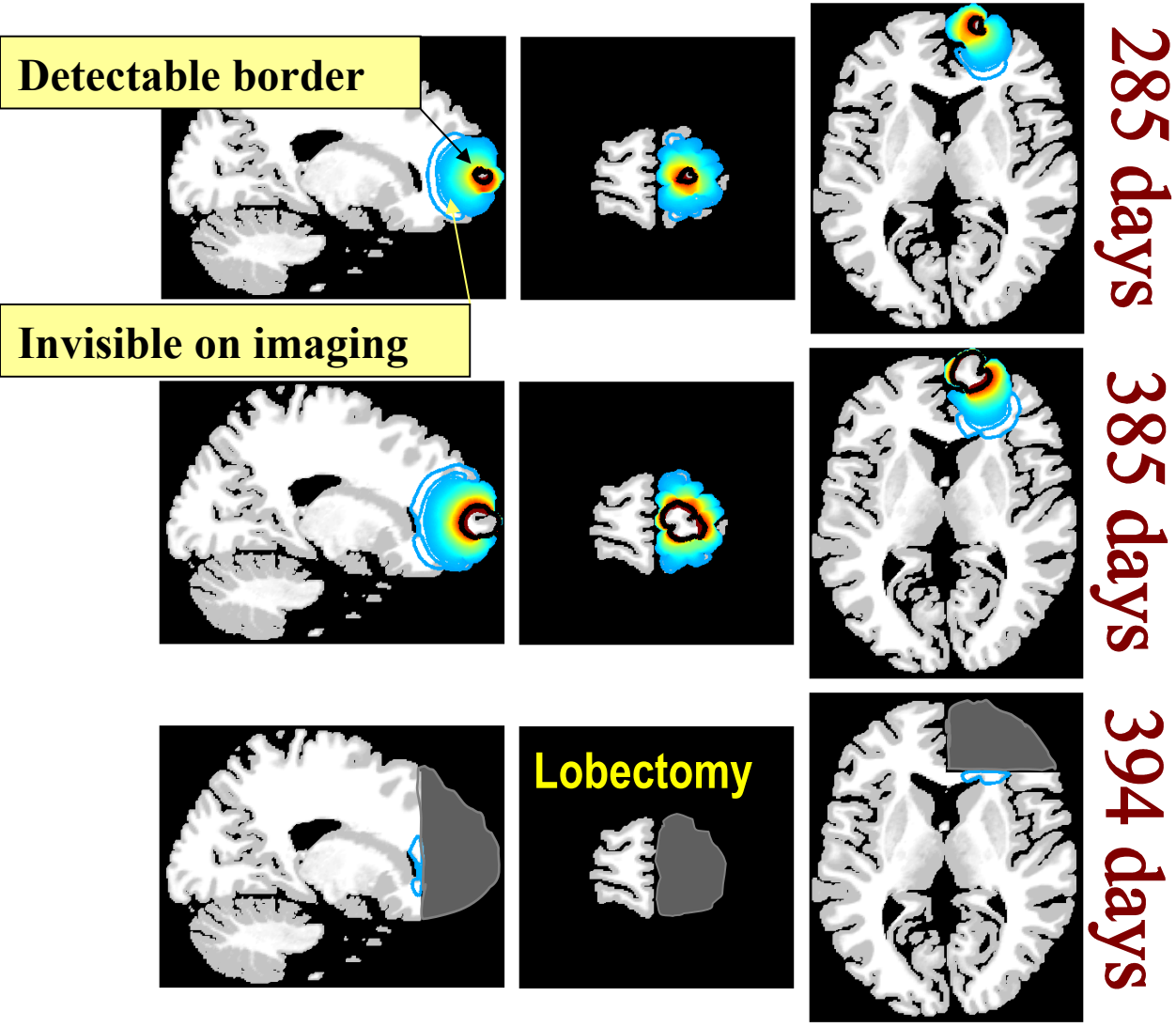
Direct problem: Foresee the future



Sagittal, coronal and axial virtual MRIs from a continuous motion picture of the recurrence of a "favorable" glioblastoma (unusually small, 1 cm in diameter, and unusually far forward in frontal polar cortex) following extensive resection of most of the frontal lobe. Thick black contours represent the edge of the gadolinium-enhanced T1-weighted MRI (T1Gd) signal. Red: high glioma cell density; Blue: low density.

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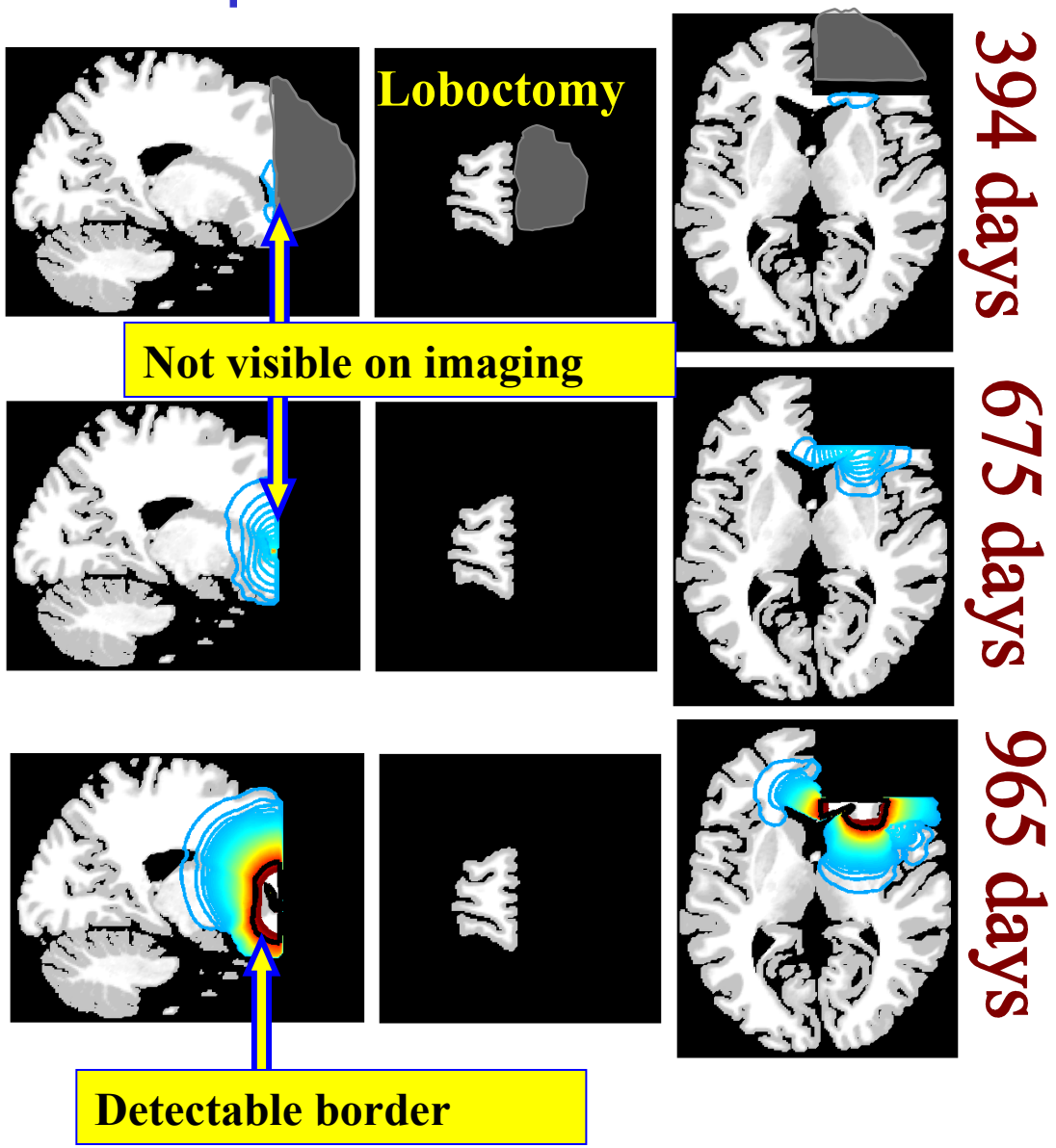
Direct problem: Foresee the future



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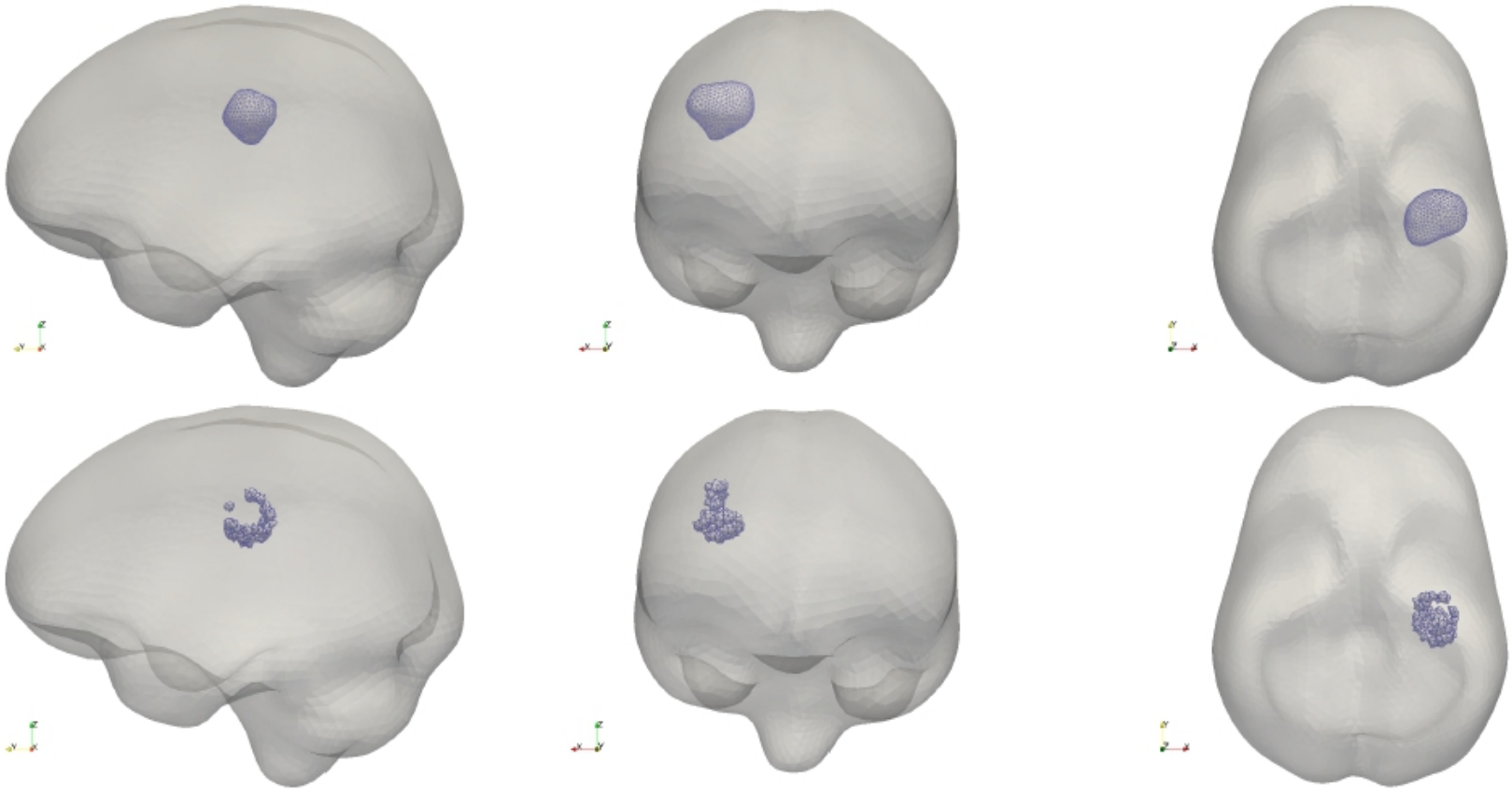
Control & optimization of chemotherapy

Giverso, Agosti, Ciarletta, Ambrosi, *ZAMM* (2018)

Tumour mesh

Resected tumour



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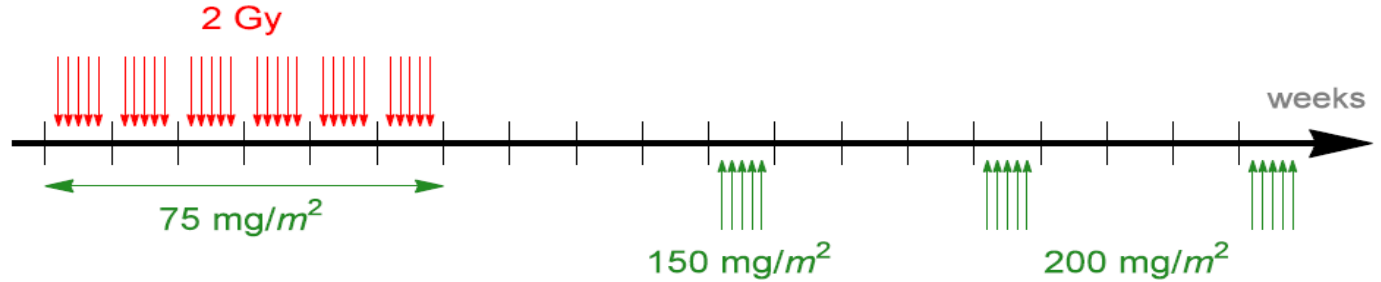
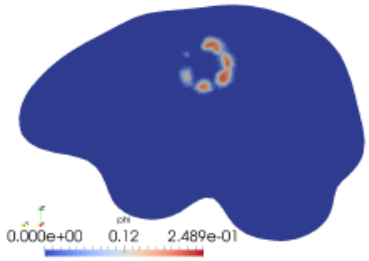
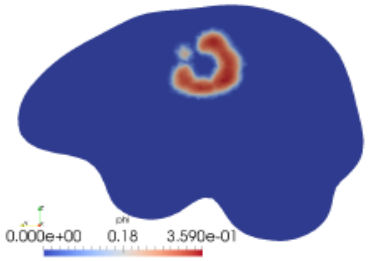
Control & optimization of chemotherapy

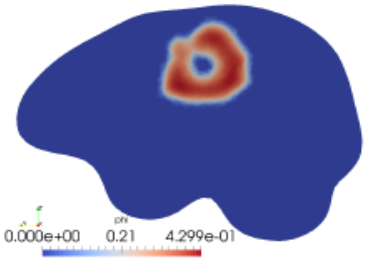
Standard Stupp protocol:

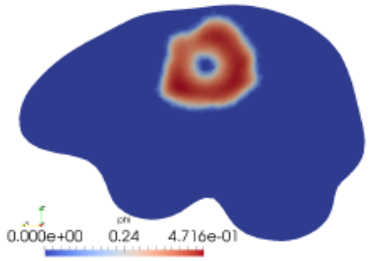


Standard therapy

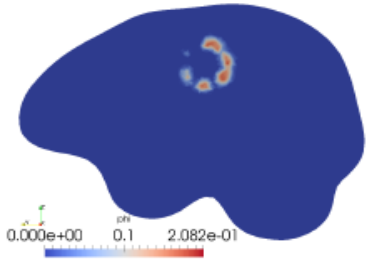


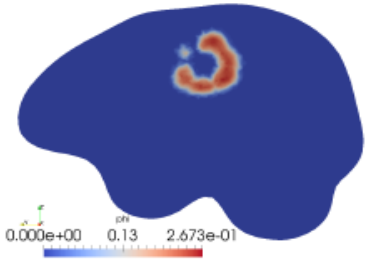


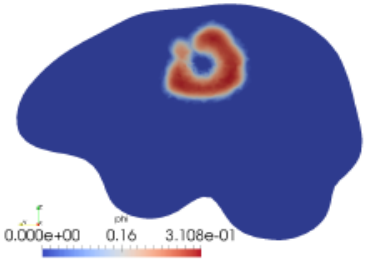


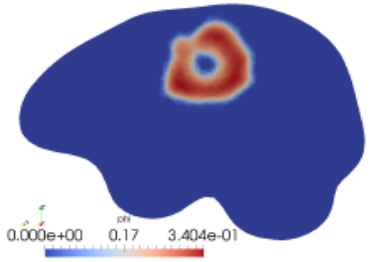


Increased CHT dose

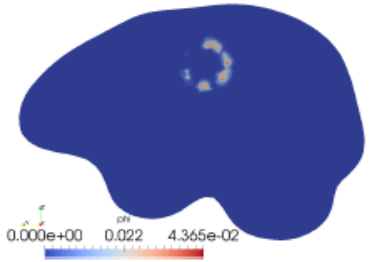


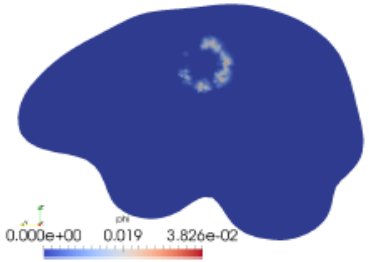


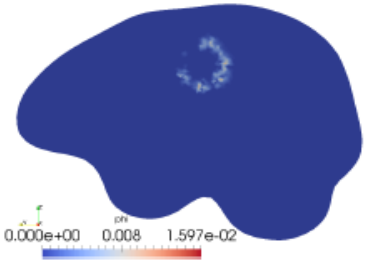


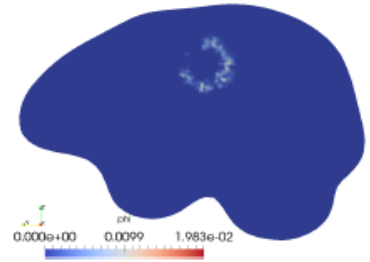


Increased RT sensitivity









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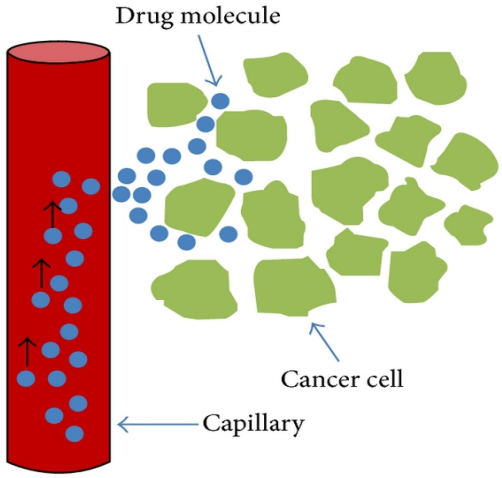
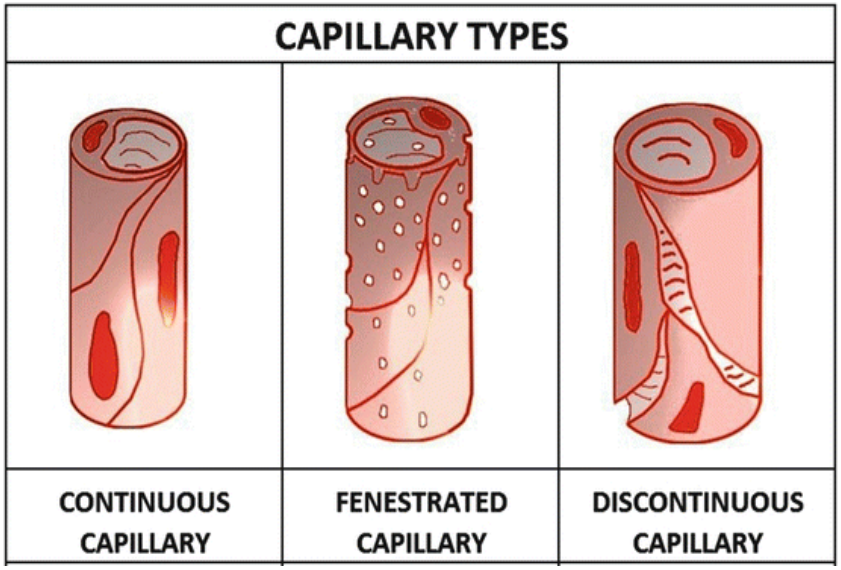
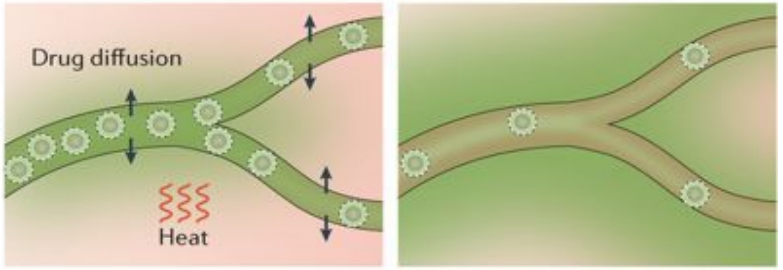
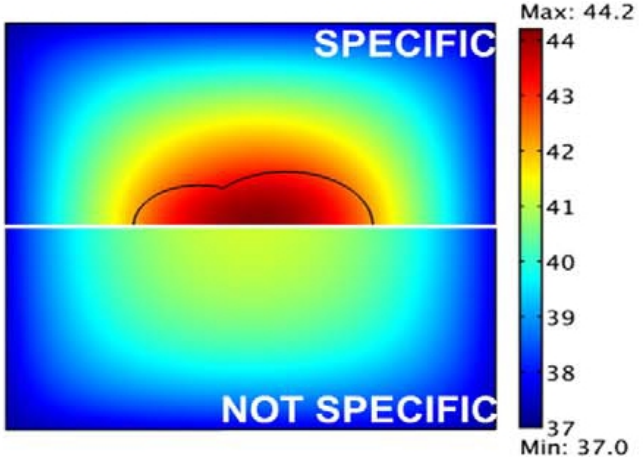
Hyperthermic treatment of tumours





Cervadoro, Giverso, …, L.P., & Decuzzi, *PLOS One* **8**, E57332 (2012)

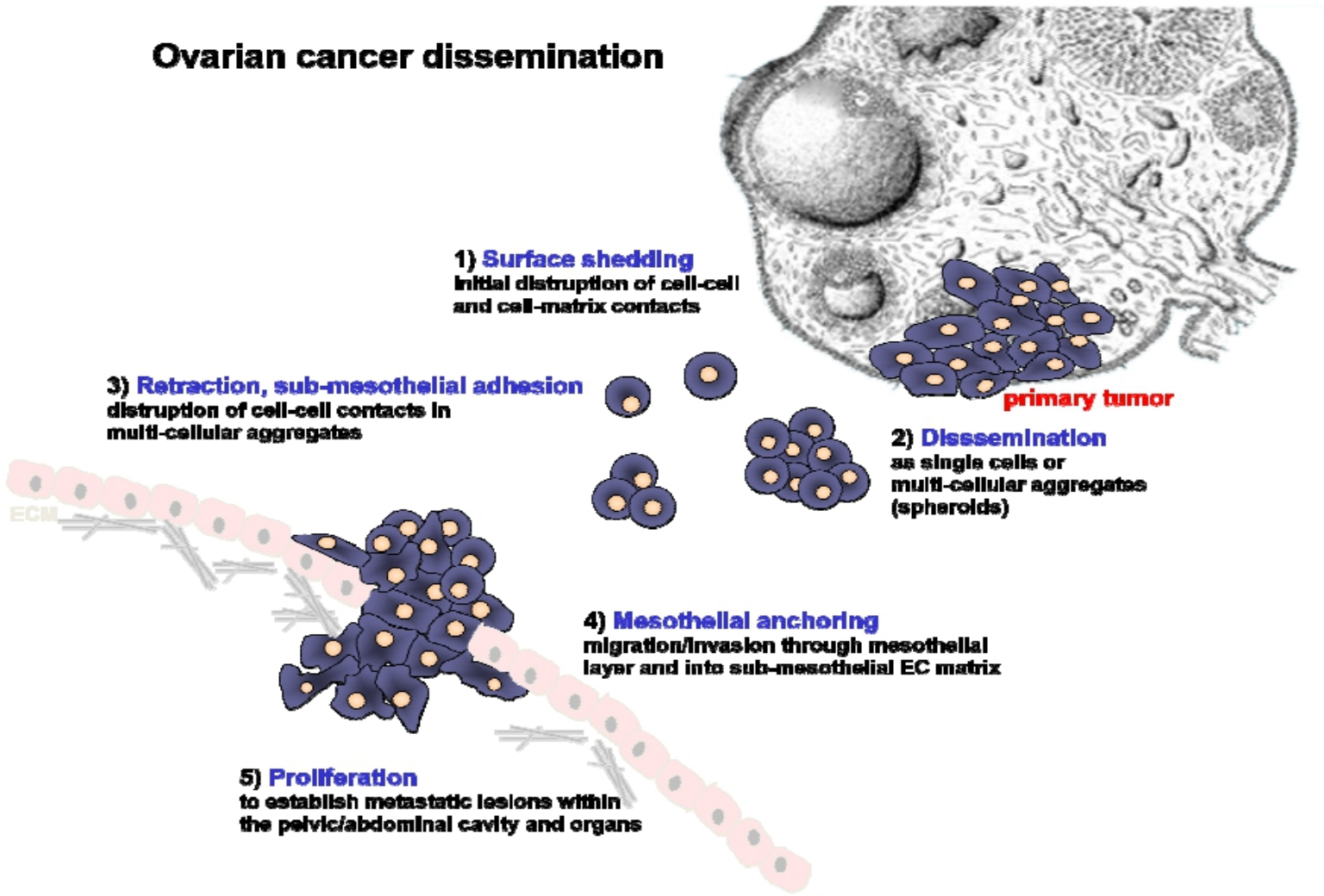




POLITECNICO DI TORINO

Invasion of Ovary Cancer Cells

Lab. di Immunogenetica Ospedale Molinette



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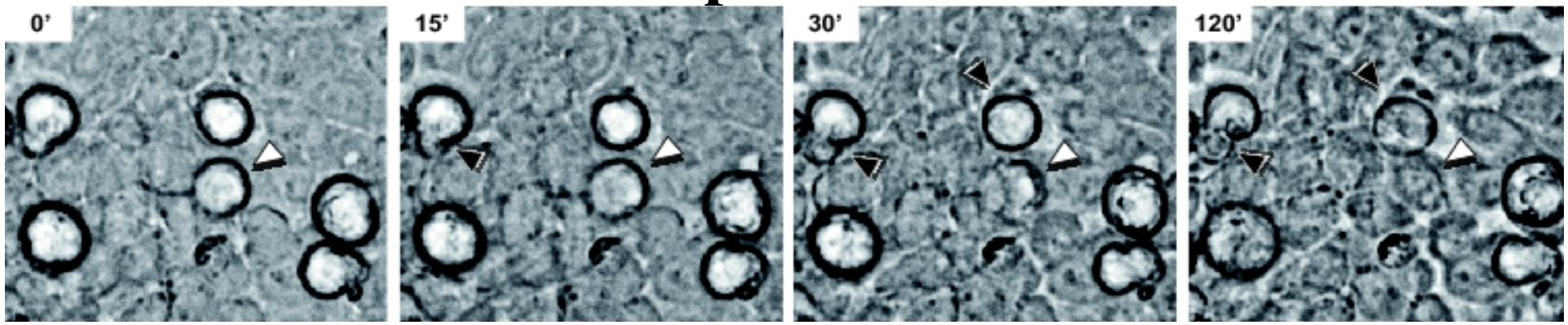
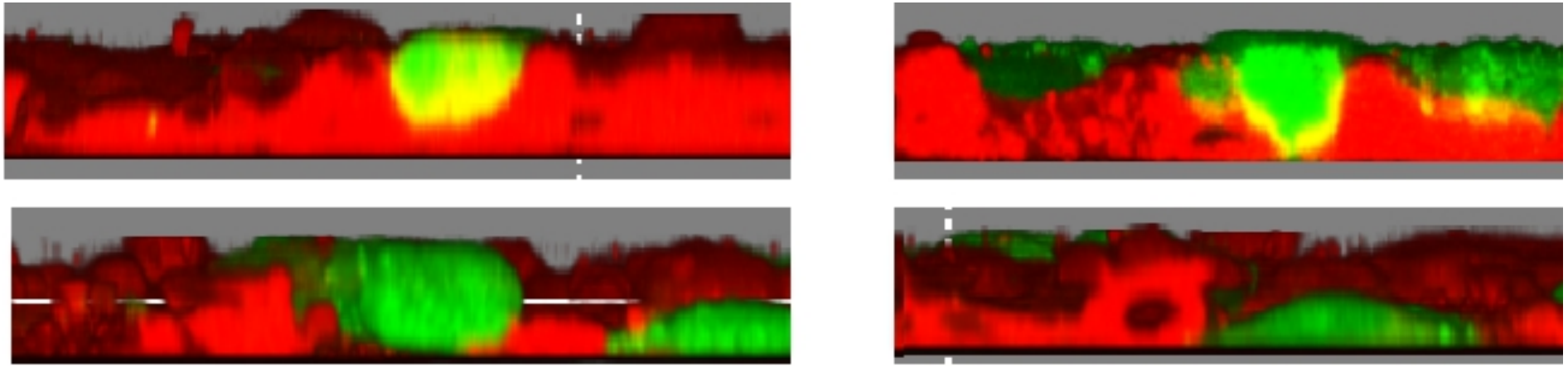
Invasion of Ovary Cancer Cells

Top view



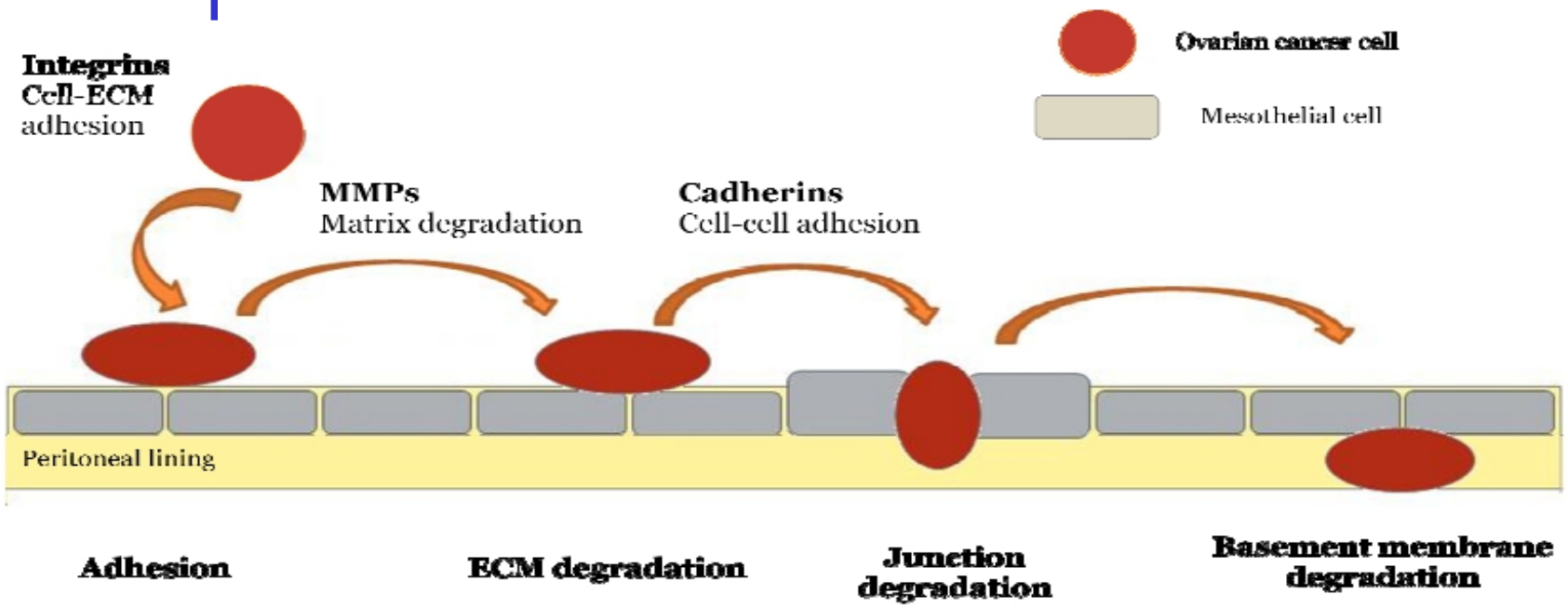
Side view

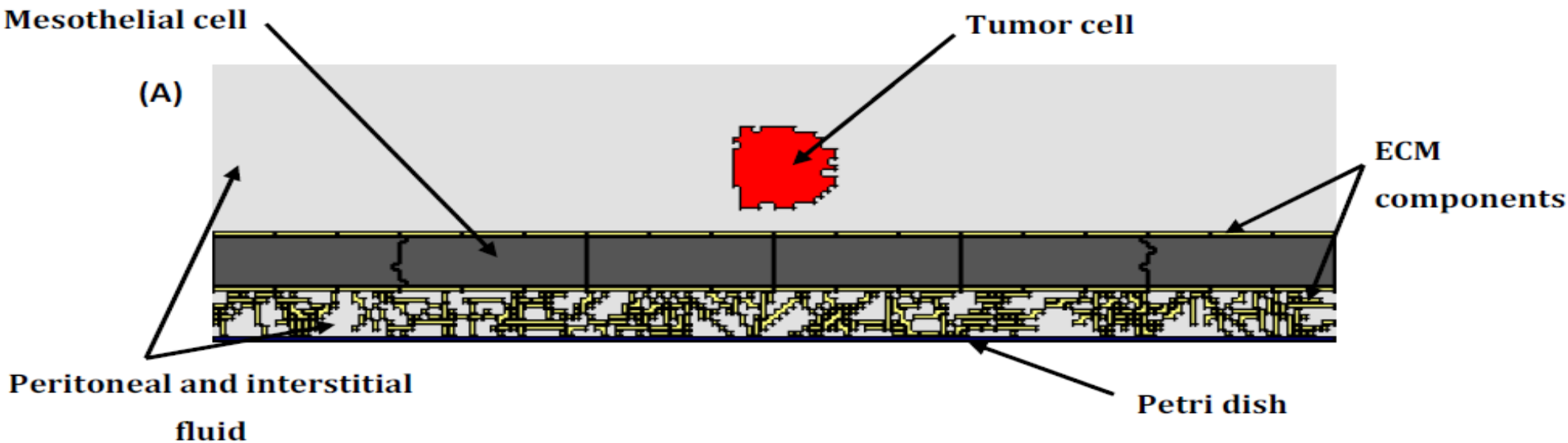


Giverso, Scianna, L.P., Lo Buono & Funaro, *Math. Model. Nat. Phenom.* **5**, 203-223 (2010)

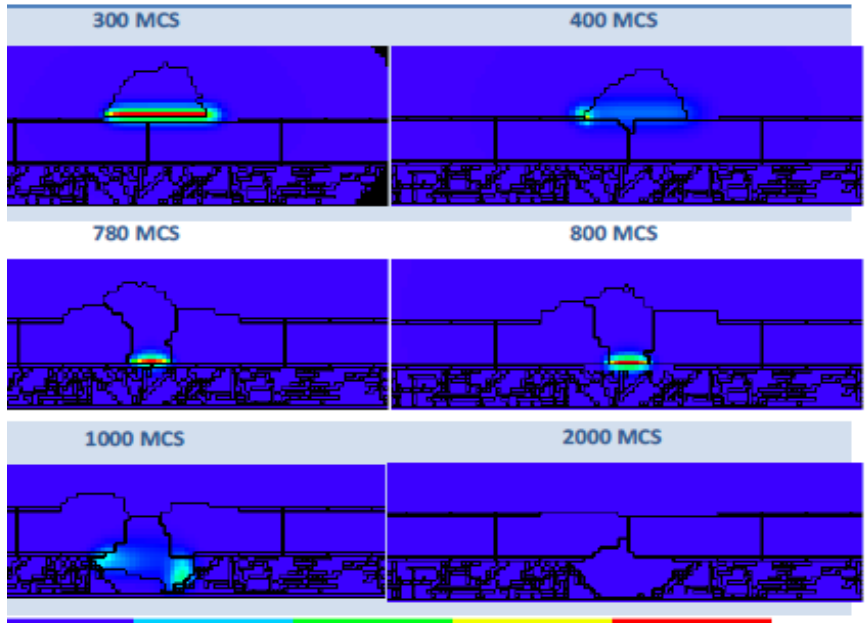
POLITECNICO DI TORINO

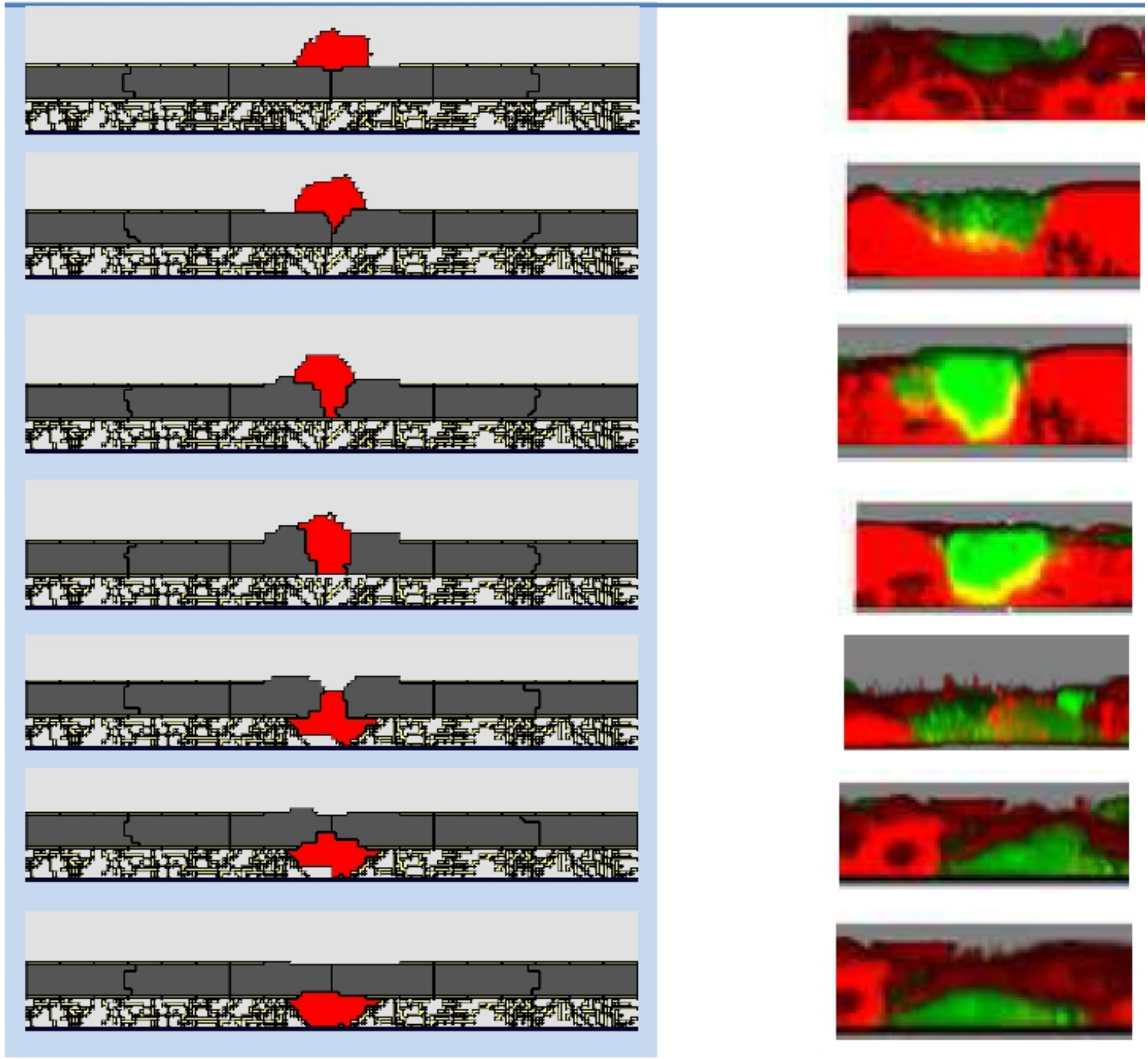
Invasion of Ovary Cancer Cells






0 MCS
200 MCS
400 MCS
600 MCS
700 MCS
750 MCS
800 MCS
1000 MCS
1200 MCS
1400 MCS
1600 MCS
1800 MCS
2000 MCS
5000 MCS


300 MCS
400 MCS
780 MCS
800 MCS
1000 MCS
2000 MCS



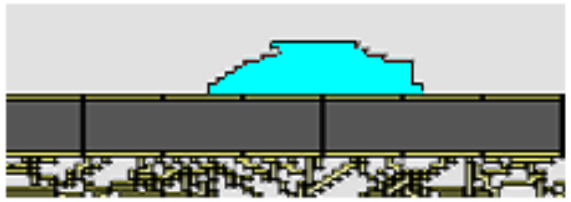
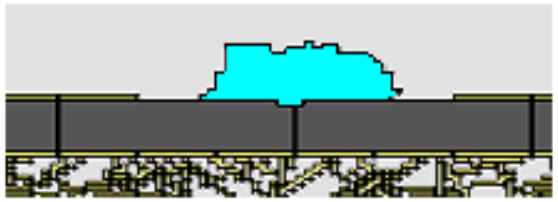
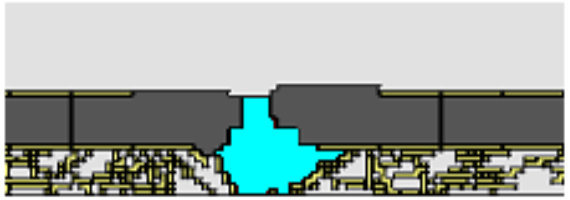
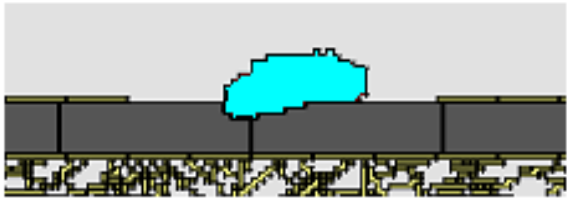
POLITECNICO DI TORINO

Invasion of Ovary Cancer Cells

Metallo-proteinases

Mesothelial adhesion

Cell-mesothelial adhesion

Parameter	Low	High
ϑ_{MMP}	5000 MCS 	180 MCS 
$J_{m,m}$	5000 MCS 	400 MCS 
$J_{c,m}$	5000 MCS 	5000 MCS 

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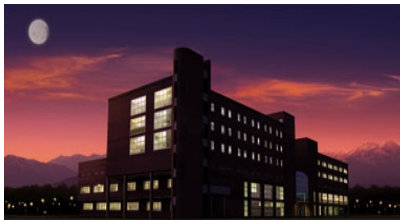
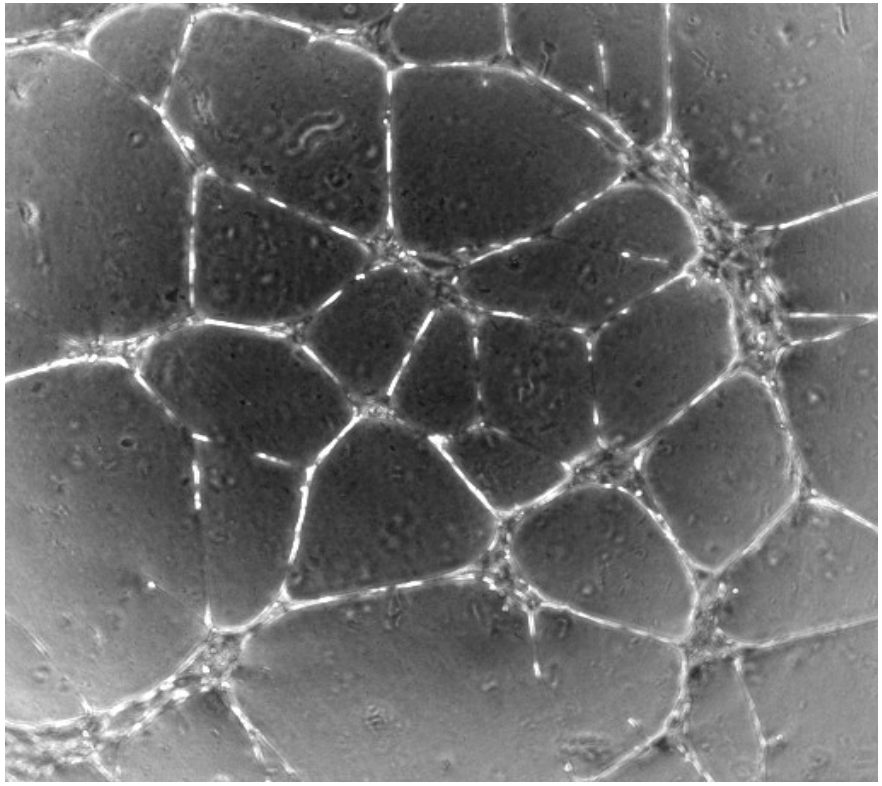
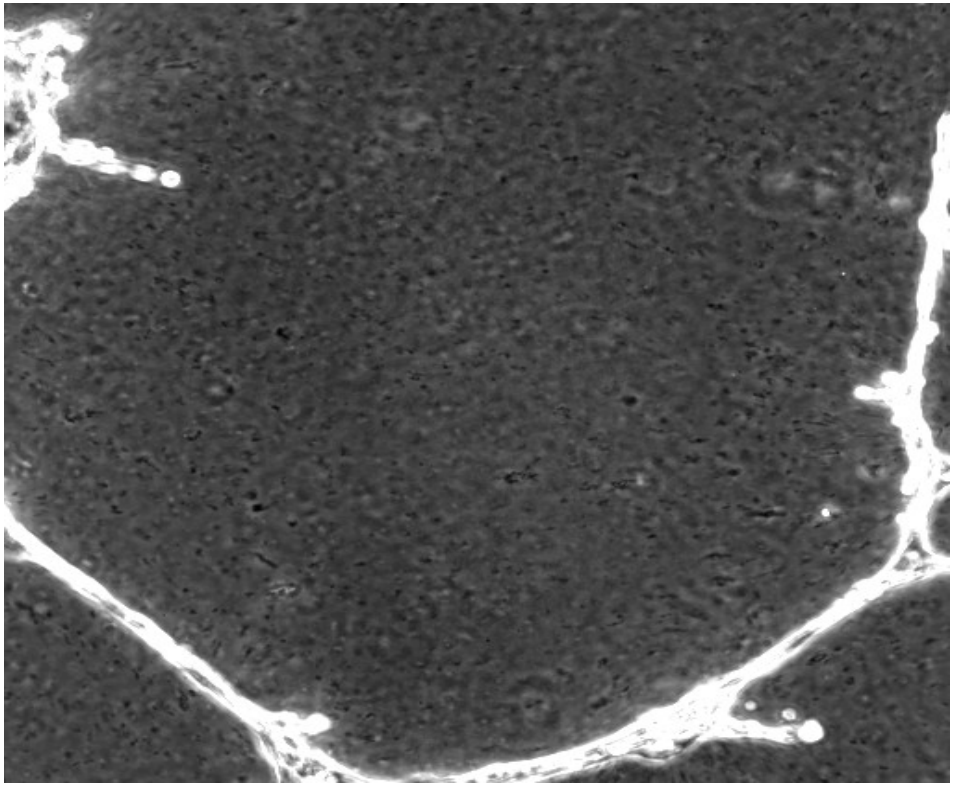
Modelling vasculogenesis



Istituto per la Ricerca e la Cura del Cancro





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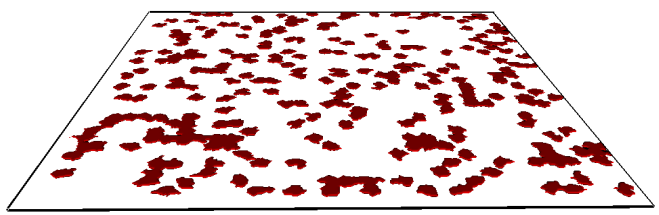
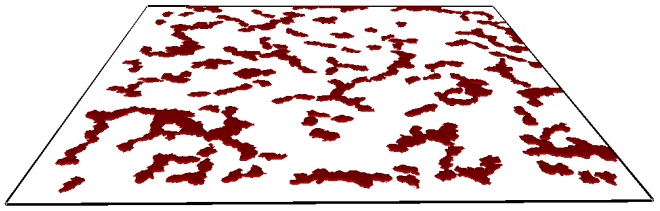
IBM for vasculogenesis

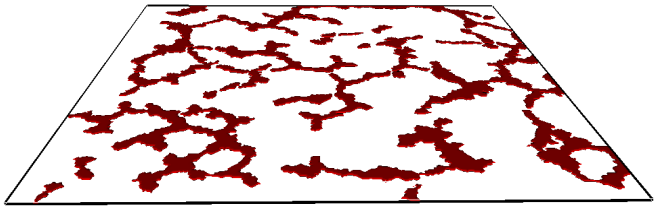


50 px ≈ 50 μm

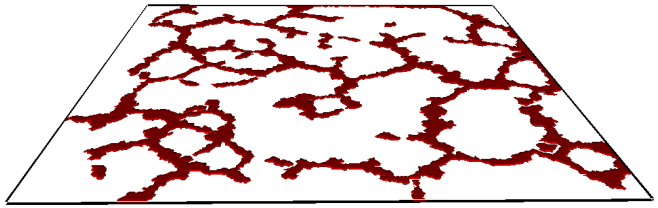
(A)



(B)



(C)



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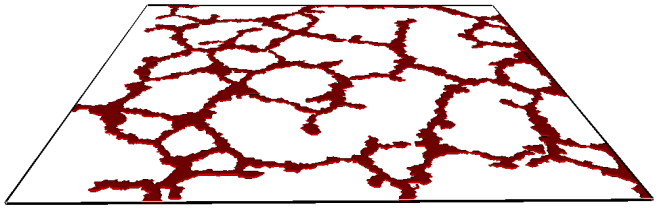
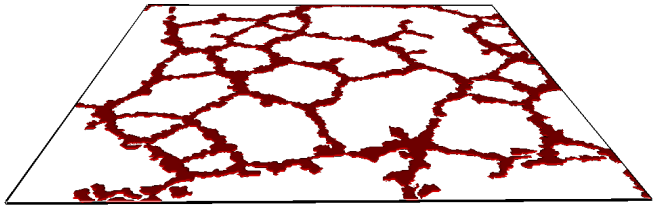
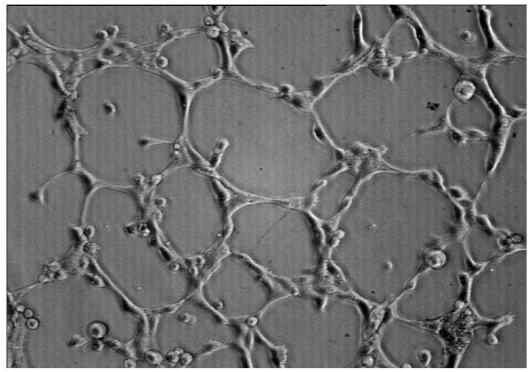


(E)



(F)



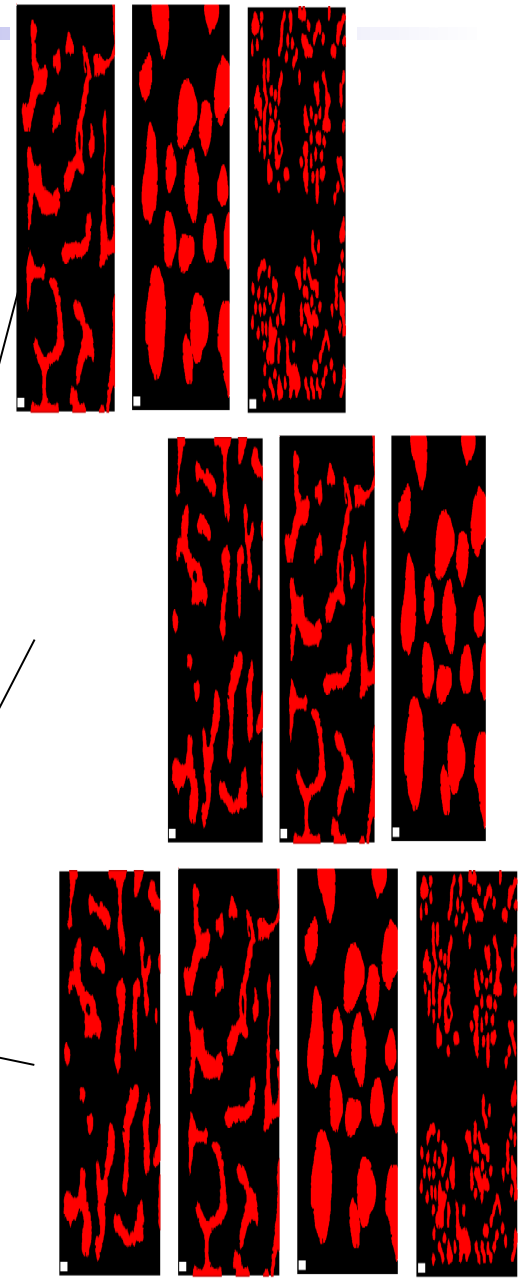
(G)

Scianna, Munaron & L.P., *Progr. Biophys. Molec. Biol.* **106**, 450-462 (2011)

POLITECNICO DI TORINO

IBM for vasculogenesis

POTENTIAL THERAPIES			
BIOLOGICAL MECHANISM	**MODEL PARAMETER**	**EFFICIENCY**	**TOTAL TUBULE LENGTH (μm)**
VEGF UPTAKE	β_V	+++	
VEGF DEGRADATION	λ_V	++	
CALCIUM ENTRY	F_{AA} , F_{NO}	+++	
AA PRODUCTION	v_{AA} , c_{AA}	+	
NO PRODUCTION	$v_{Ca\text{-}AA}$, v_{NO}	+	
PERSISTENCE	$\mu_{in}(\cdot)$	++	
CHEMOTAXIS	μ_{ch}	+++	
ADHESION	$J^{ext}((\cdot,C),(\cdot,C))$	+++	
CONTROL			



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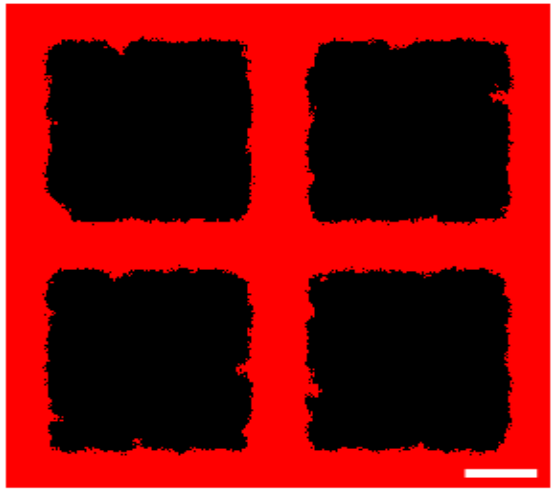
IBM for angiogenesis



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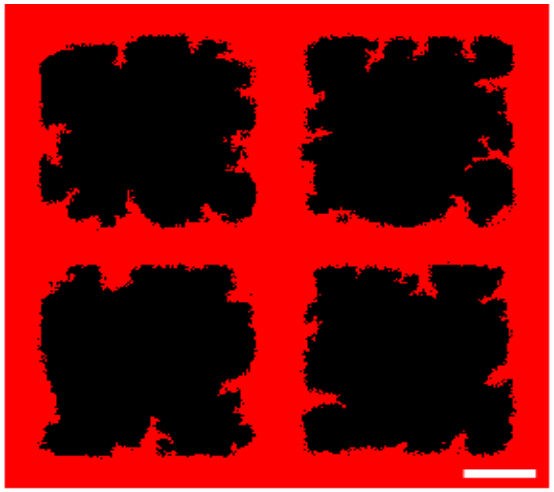

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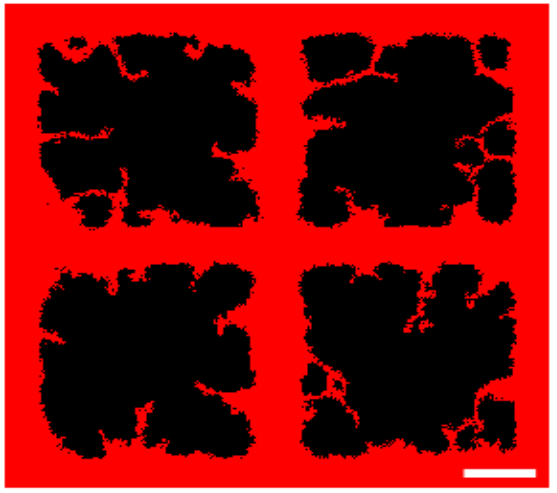

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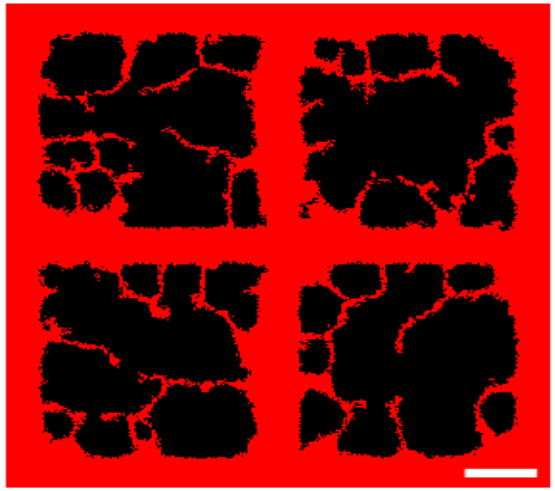

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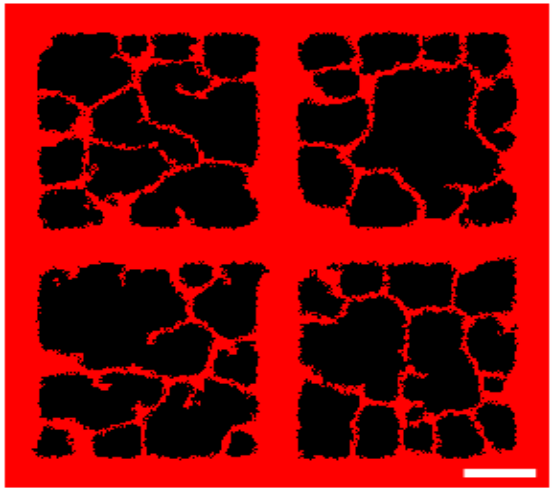

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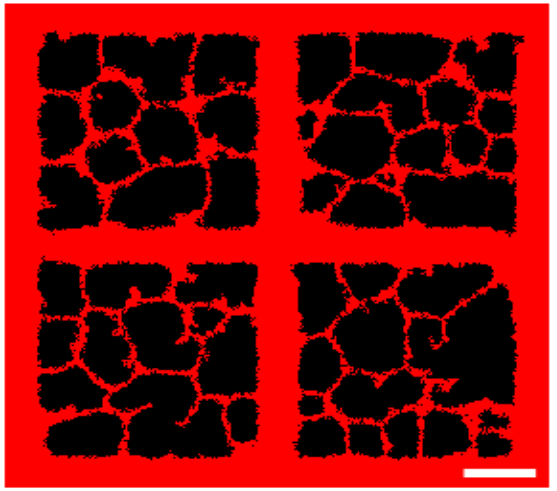

72 h

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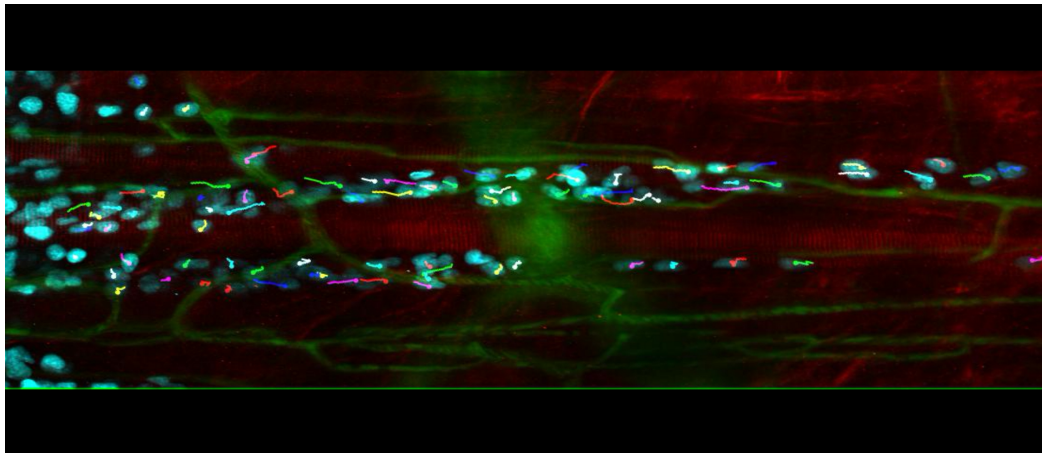
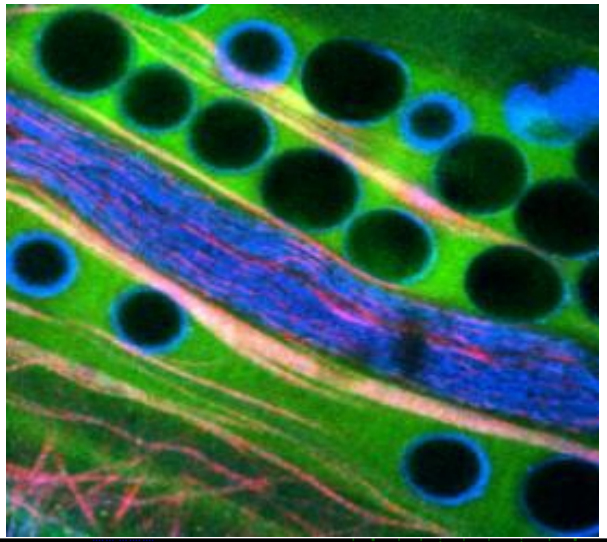
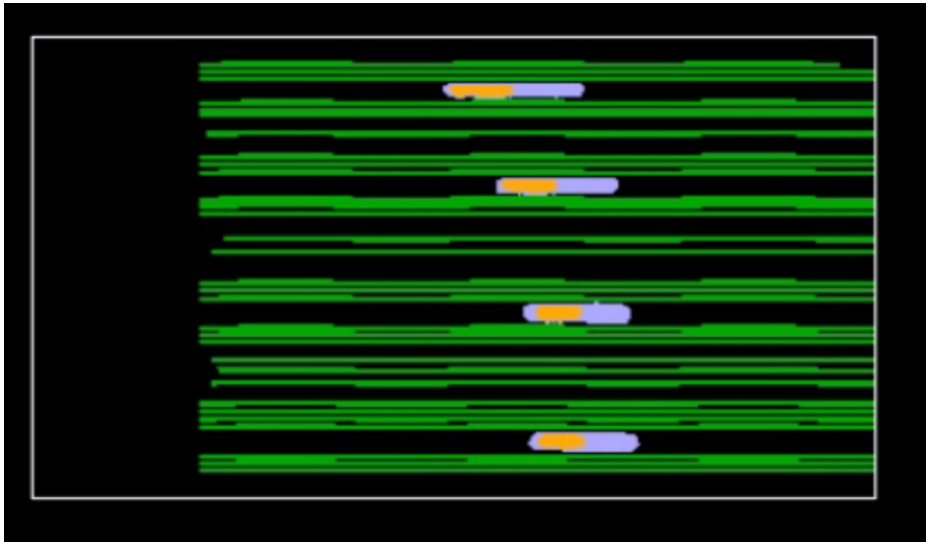
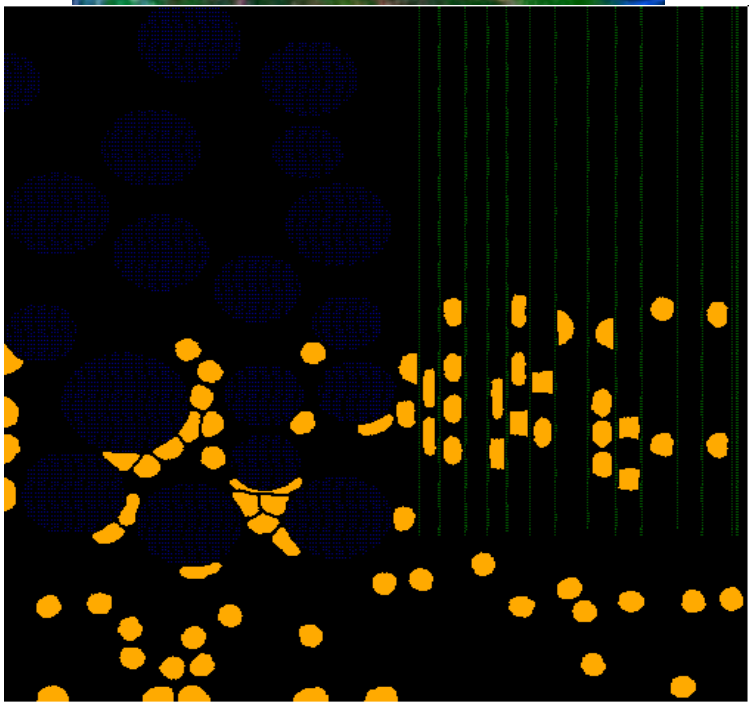
Invasion of tissues in vivo









Weigelin, Scianna, L.P. & Friedl (in press)

POLITECNICO DI TORINO

How Can Mathematical Models Support Cancer Research?

- Organizing genomic and proteomic data
- Extrapolating invisible features from imaging
- Inferring the past evolution of diseases
- Foreseeing future evolutions
- Optimizing & personalizing therapies

Very strong interaction required
Researchers in maths and bio-medicine at the same bench

Thank you for the attention

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