UNIVERSITÀ DEL SALENTO

Multiphase modeling of porous media

from concrete to tumor growth

Giuseppe Sciumè

Department of Innovation Engineering, University of Salento, Italy

Co-tutelage PhD agreement between University of Padua & ENS de Cachan

PhD directors: Bernhard Schrefler and Yves Berthaud

Concrete at early age

- Outline of the general mathematical model
- Relevant hydration-dependent constitutive relationships
- Applications: massive structures and repairs

Tumor growth

General conclusions

Massive structures

TCM models

Other concrete structures

Thin structures

HCM models

THCM

Assumptions **unidirectional coupling THC→M:**

- *partial saturation*
- *small displacements and small crack opening*

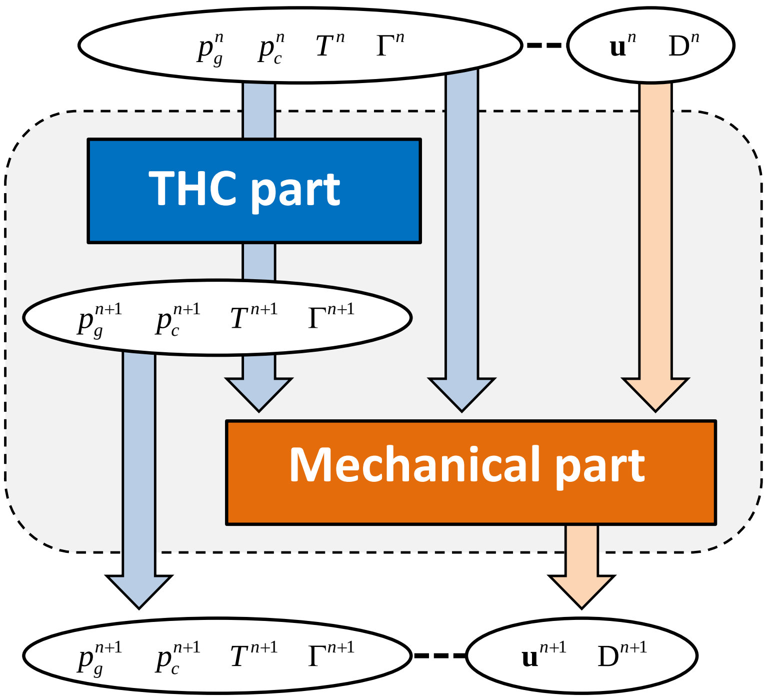
Peculiarities of the model

- Effect of age on the desorption isotherm and Biot's coefficient
- Autogenous and drying shrinkage computed in a unified way
- Mechanical damage coupled with creep
- 3D implementation in Cast3M that simplifies model exploitation

Background:

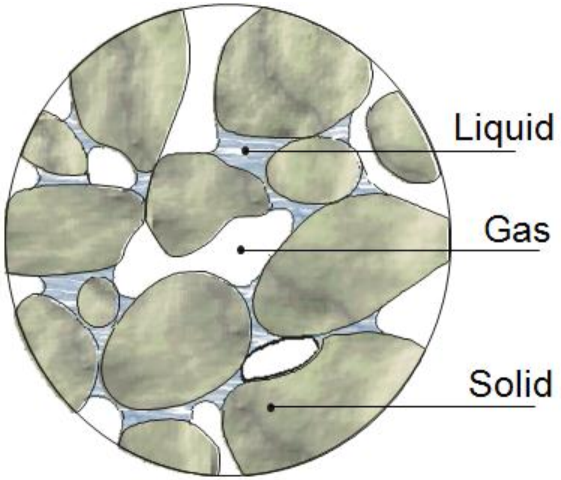
Gawin D., Pesavento F., Schrefler B. (2006)

Benboudjema F. and Torrenti J-M (2008)



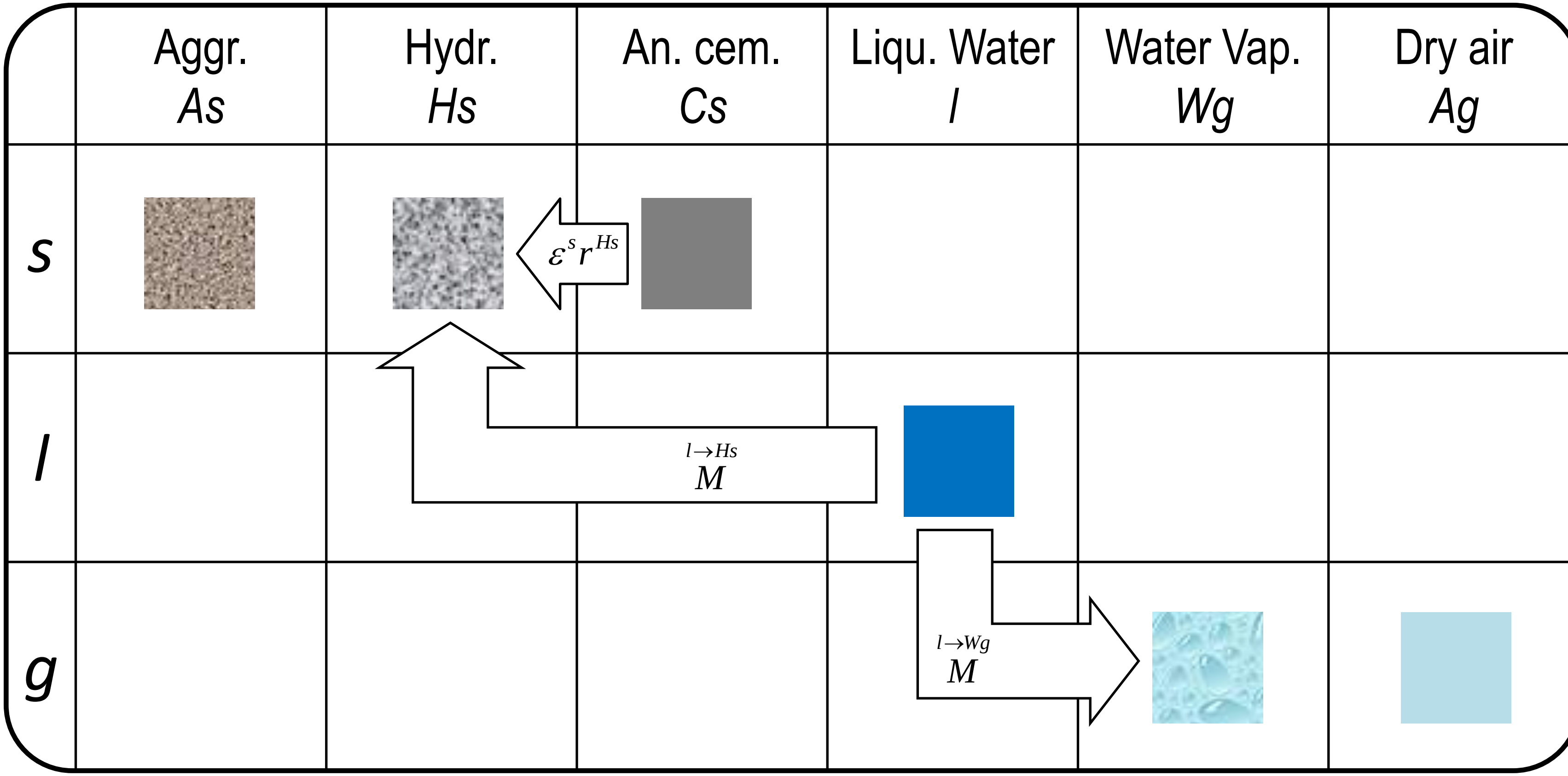
The MULTIPHASE system

Concrete is treated as a **porous solid** and porosity is denoted by ε, so that the volume fraction occupied by the solid skeleton is $\varepsilon^s = 1 - \varepsilon$.
The rest of the volume is occupied by the liquid water (ε^l); and the gaseous phase (ε^g).



1 Solid phase *s*:	• Anhydrous cement: *Cs* • Aggregates: *As* • Hydrates: *Hs*
1 Liquid phase *l*:	• Liquid water
1 Gaseous phase *g*:	• Water vapour: *Wg* • Dry air: *Ag*

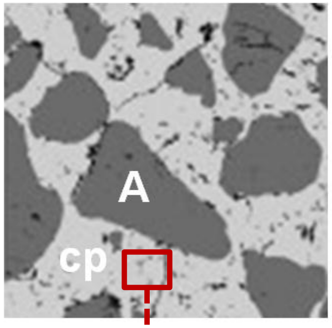
Mass exchanges $\overset{\alpha \to \beta}{M}$ and reaction terms $\varepsilon^{s} r^{Hs}$



$\varepsilon^{s} r^{Hs}$ hydration rate of the anhydrous cement

$\overset{l \to Hs}{M}$ chemically combined water and $\overset{l \to Wg}{M}$ vaporized water *per* second

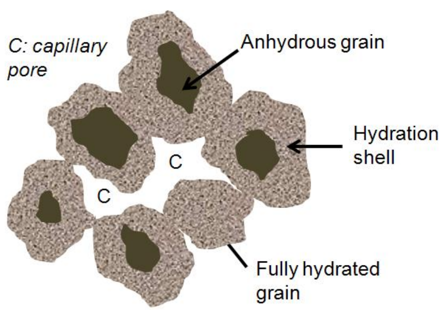
Mass balance equations: SOLID PHASE [*s*]

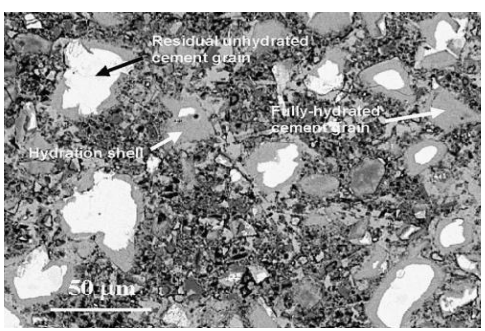


Concrete:

Aggregates (A)
+
cement paste (cp)

Cement paste





Intra-phase exchange of mass

Anhydrous cement: $$\frac{\partial\left(\varepsilon^s\rho^s\omega^{\overline{C}s}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^s\rho^s\omega^{\overline{C}s}\mathbf{v}^{\bar{s}}\right)+\varepsilon^s r^{Hs}=0$$

Aggregates: $$\frac{\partial\left(\varepsilon^s\rho^s\omega^{\overline{A}s}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^s\rho^s\omega^{\overline{A}s}\mathbf{v}^{\bar{s}}\right)=0$$

Intra-phase exchange of mass

Hydration products: $$\frac{\partial\left(\varepsilon^s\rho^s\omega^{\overline{H}s}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^s\rho^s\omega^{\overline{H}s}\mathbf{v}^{\bar{s}}\right)-\varepsilon^s r^{Hs}-\overset{l\rightarrow Hs}{M}=0$$

Inter-phase exchange of mass

Summing the previous three equations gives:

$$\frac{\partial\left(\varepsilon^s\rho^s\right)}{\partial t}+\nabla\cdot\left(\varepsilon^s\rho^s\mathbf{v}^{\bar{s}}\right)=\overset{l\rightarrow Hs}{M}$$

Mass balance equations: LIQUID PHASE [*l*]

$$\frac{\partial\left(\varepsilon^l \rho^l\right)}{\partial t} + \nabla\cdot\left(\varepsilon^l \rho^l \mathbf{v}^{\bar{l}}\right) = -\overset{l\rightarrow Hs}{M} - \overset{l\rightarrow Wg}{M}$$

Mass balance equations: GAZEOUS PHASE [*g*]

Vapour water:

$$\frac{\partial\left(\varepsilon^g \rho^g \omega^{\overline{Wg}}\right)}{\partial t} + \nabla\cdot\left(\varepsilon^g \rho^g \omega^{\overline{Wg}} \mathbf{v}^{\bar{g}}\right) + \nabla\cdot\left(\varepsilon^g \rho^g \omega^{\overline{Wg}} \mathbf{u}^{\overline{\overline{Wg}}}\right) = \overset{l\rightarrow Wg}{M}$$

Dry air:

$$\frac{\partial\left(\varepsilon^g \rho^g \omega^{\overline{Ag}}\right)}{\partial t} + \nabla\cdot\left(\varepsilon^g \rho^g \omega^{\overline{Ag}} \mathbf{v}^{\bar{g}}\right) + \nabla\cdot\left(\varepsilon^g \rho^g \omega^{\overline{Ag}} \mathbf{u}^{\overline{\overline{Ag}}}\right) = 0$$

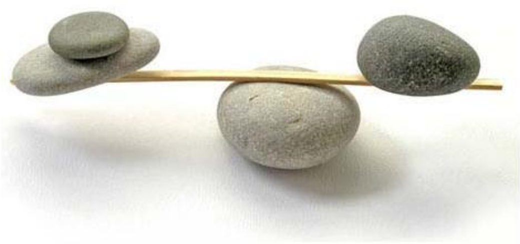
Summing the previous two equations gives:

$$\frac{\partial\left(\varepsilon^g \rho^g\right)}{\partial t} + \nabla\cdot\left(\varepsilon^g \rho^g \mathbf{v}^{\bar{g}}\right) = \overset{l\rightarrow Wg}{M}$$

Governing equations

Primary variables: p^g p^c T $\mathbf{u}$ Internal variables: Γ D

MASS BALANCE EQUATIONS:



Dry air

$$\frac{\partial\left(\varepsilon^g\rho^g\omega^{\overline{Ag}}\right)}{\partial t}-\nabla\cdot\left(\rho^{gA}\frac{k_{rel}^g\mathbf{k}}{\mu^g}\nabla p^g\right)+\nabla\cdot\left[\rho^g\frac{M_AM_W}{M_g^2}D^{\overline{Wg}}\nabla\left(\frac{p^{gW}}{p^g}\right)\right]=0$$

Water (liquid + vapour):

$$\frac{\partial\left(\varepsilon^l\rho^l\right)}{\partial t}+\frac{\partial\left(\varepsilon^g\rho^g\omega^{\overline{Wg}}\right)}{\partial t}-\nabla\cdot\left[\rho^l\frac{k_{rel}^l\mathbf{k}}{\mu^l}\nabla\left(p^g-p^c\right)\right]-\nabla\cdot\left(\rho^{gW}\frac{k_{rel}^g\mathbf{k}}{\mu^g}\nabla p^g\right)-\nabla\cdot\left[\rho^g\frac{M_AM_W}{M_g^2}D^{\overline{Wg}}\nabla\left(\frac{p^{gW}}{p^g}\right)\right]=-\overset{l\rightarrow Hs}{M}$$

ENTHALPY BALANCE EQUATION:

$$\left(\rho C_p\right)_{\text{eff}}\frac{\partial T}{\partial t}-\nabla\cdot\left(\chi_{\text{eff}}\nabla T\right)=L_{hydr}\frac{\mathrm{d}\Gamma}{\mathrm{d}t}+H_{vap}\frac{\partial\left(\varepsilon^l\rho^l\right)}{\partial t}+H_{vap}\overset{l\rightarrow Hs}{M}-H_{vap}\nabla\cdot\left[\rho^l\frac{k_{rel}^l\mathbf{k}}{\mu^l}\nabla\left(p^g-p^c\right)\right]$$

LINEAR MOMENTUM BALANCE EQUATION:

$$\nabla\cdot\left(\frac{\partial\mathbf{t}}{\partial t}\right)+\frac{\partial\rho}{\partial t}\mathbf{g}=0$$

The hydration model

$$\Gamma_{(t)} = \frac{m_{(t)}^{hydr}}{m_{\infty}^{hydr}}$$

Degree of reaction (hydration advancement)

With: $m_{(t)}^{hydr}$ *chemically combined water mass at time t*

m_{∞}^{hydr} *chemically combined water mass at time t = ∞*

Arrhenius type law with the rate of hydration is a function of:

- Hydration degree
- relative humidity
- temperature

$$\frac{d\Gamma}{dt} = A_{(\Gamma)} \beta_{(h)} \exp\left(-\frac{E_a}{RT}\right)$$

with: $A_{(\Gamma)}$ *chemical affinity*

$\beta_{(h)}$ *function of relative humidity [0 – 1]*

E_a *activation energy*

Volume fractions of phases during hydration

T.C. Power model *(Enhanced by Jensen and Hansen to account silica fume, 2001)*

Chemical shrinkage: $V_{cs} = k \cdot [0,20 + 0,69 \cdot (s/c)] \cdot (1-p) \cdot \xi$

Capillary water: $V_{cw} = p - k \cdot [1,32 + 1,57 \cdot (s/c)] \cdot (1-p) \cdot \xi$

Gel water: $V_{gw} = k \cdot [0,60 + 1,57 \cdot (s/c)] \cdot (1-p) \cdot \xi$

Gel solid: $V_{gs} = k \cdot [1,52 + 0,74 \cdot (s/c)] \cdot (1-p) \cdot \xi$

Cement: $V_{c} = k \cdot (1-p) \cdot (1-\xi)$

Silica fume: $V_{cs} = k \cdot [1,43 \cdot (s/c)] \cdot (1-p) \cdot (1-\xi)$

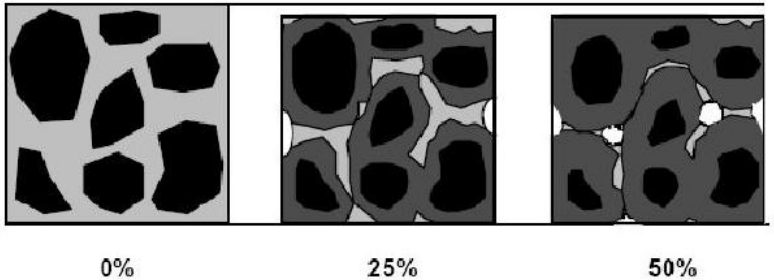
Cement paste

- Porosity function
- Self-desiccation
- Autogenous shrinkage

obtained from stochiometry

$$k = \frac{1}{1 + (\rho_c/\rho_s) \cdot (s/c)} \qquad p = \frac{w/c}{(w/c) + (\rho_w/\rho_c) + (\rho_w/\rho_s) \cdot (s/c)}$$

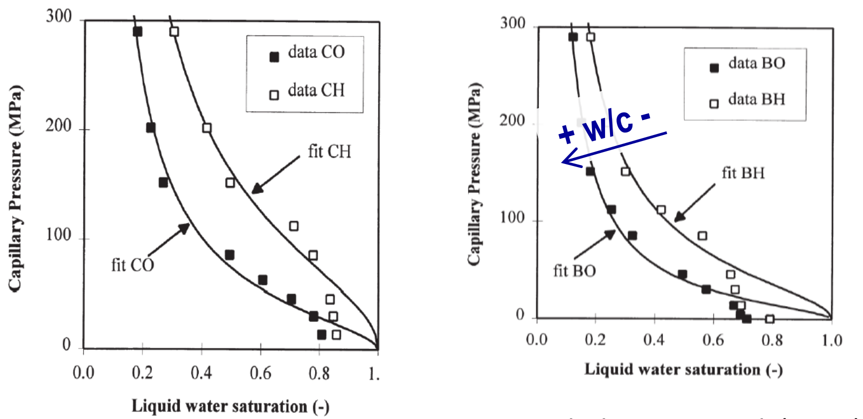
w, *c* and *s* are respectively the masses of water, cement and silica fume present in a cubic meter of concrete.



Hydration degree
and LeChatelier contraction

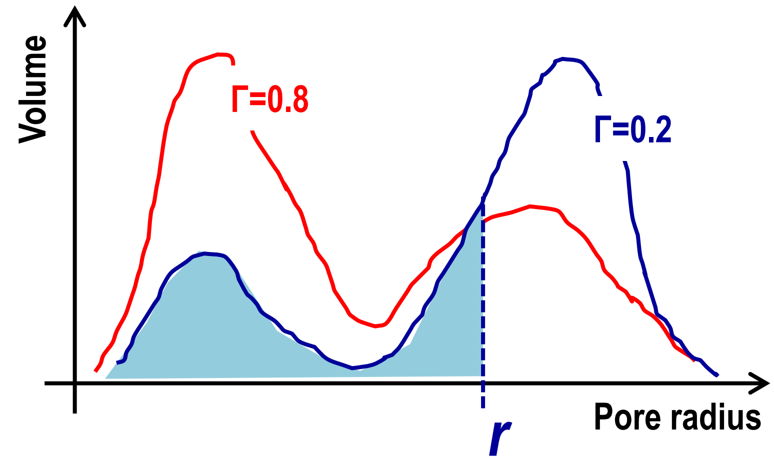
Hydration-dependent desorption isotherm

Experimental results for w/c impact



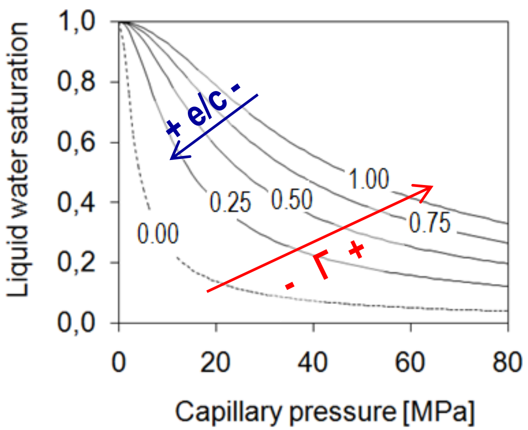
Baroghel-Bouny *et al.* (1999)

Porosity evolution



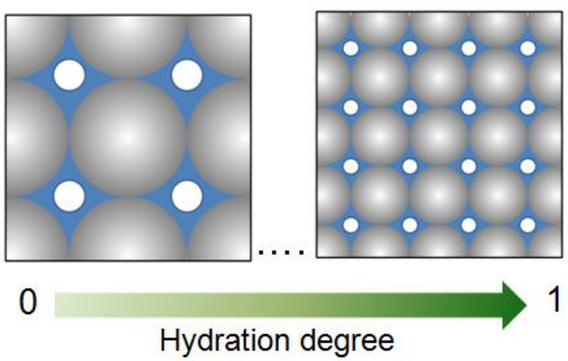
Parallelism

Laplace's equation



Van Genuchten (readapted):

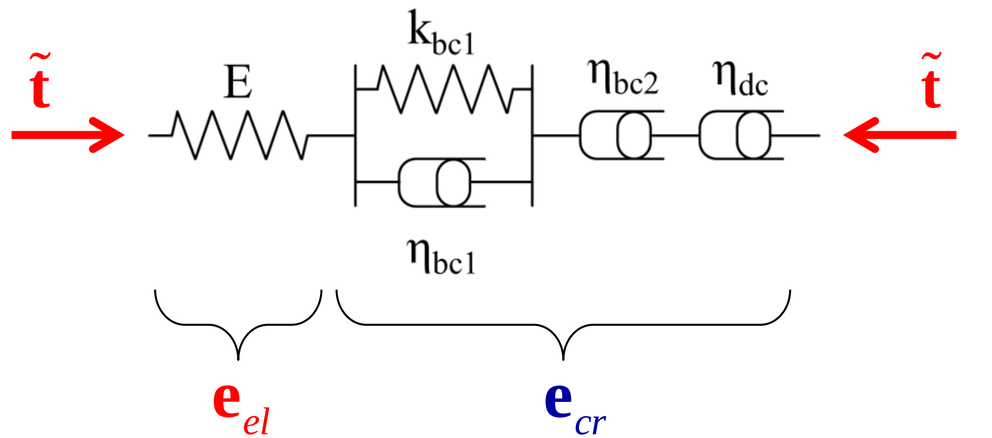
$$S_w = \left\{ 1 + \left[\frac{p_c}{a} \left(\frac{\Gamma + \Gamma_i}{1 + \Gamma_i} \right)^{-c} \right]^{\frac{b}{b-1}} \right\}^{-\frac{1}{b}}$$



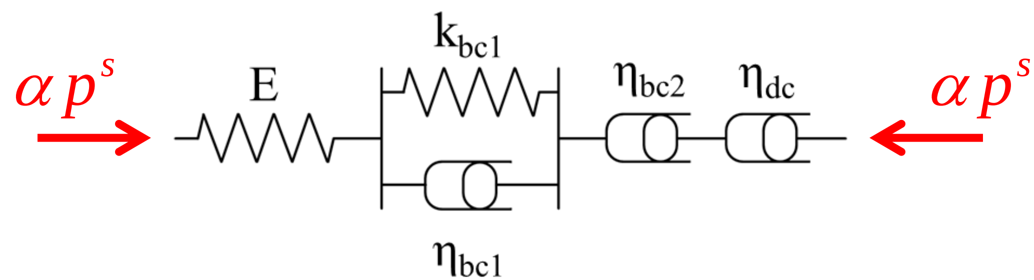
Visco-elastic damageable model

$\tilde{\mathbf{t}}$ is the effective stress (in the sense of damage mechanics):

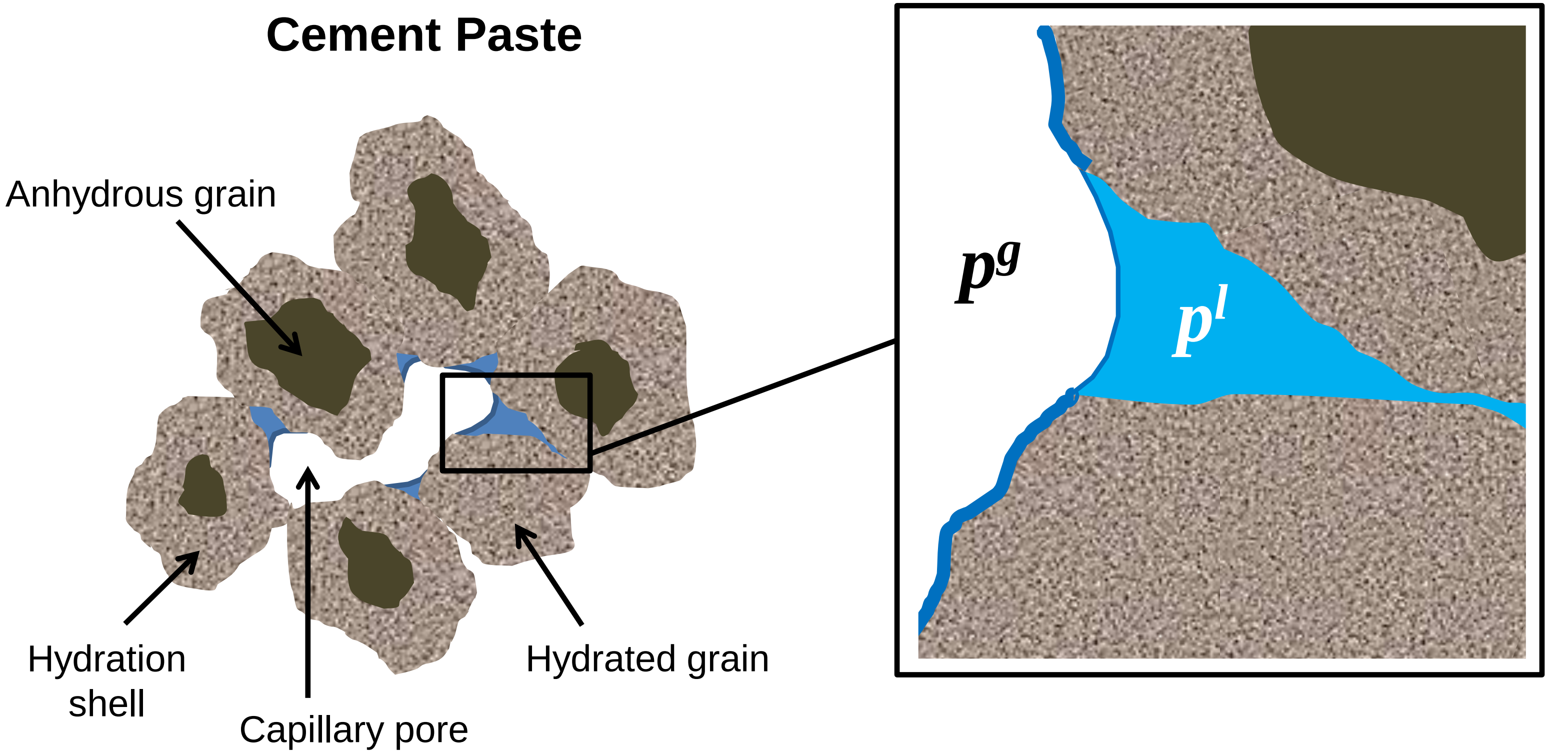
$$\mathbf{t} = (1 - D)\tilde{\mathbf{t}}$$



Shrinkage computed consistently with the effective stress principle of porous media mechanics.



$$\dot{\tilde{\mathbf{t}}} = \mathbf{E}_{(\Gamma)}\dot{\mathbf{e}}_{el} = \mathbf{E}_{(\Gamma)}\left(\dot{\mathbf{e}} - \dot{\mathbf{e}}_{th} - \dot{\mathbf{e}}_{cr} - \dot{\mathbf{e}}_{sh}\right)$$



Effective stress

in the sense of porous media mechanics

$$\mathbf{t}_{eff} = \tilde{\mathbf{t}} + \mathbf{1}\alpha p^s$$

Solid pressure

$$p^s = S^g p^g + S^l p^l = p^g - S^l p^c$$

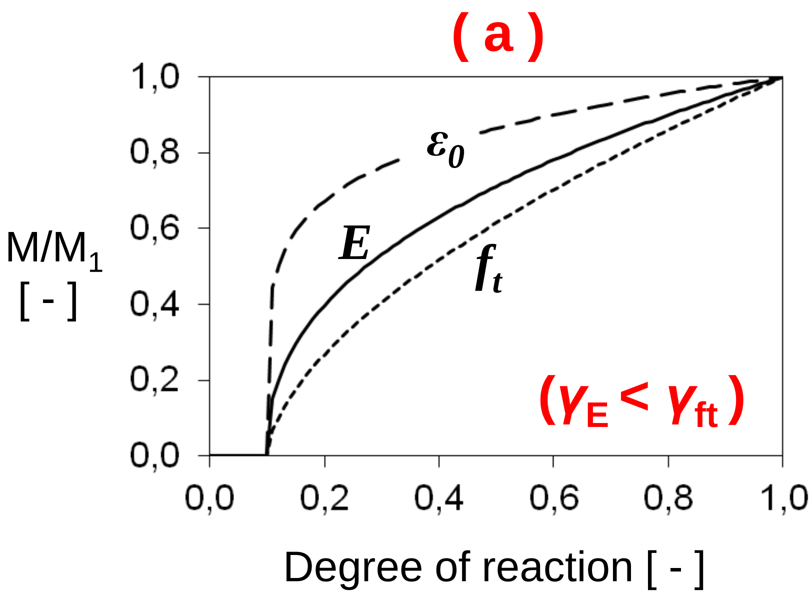
Biot's coefficient

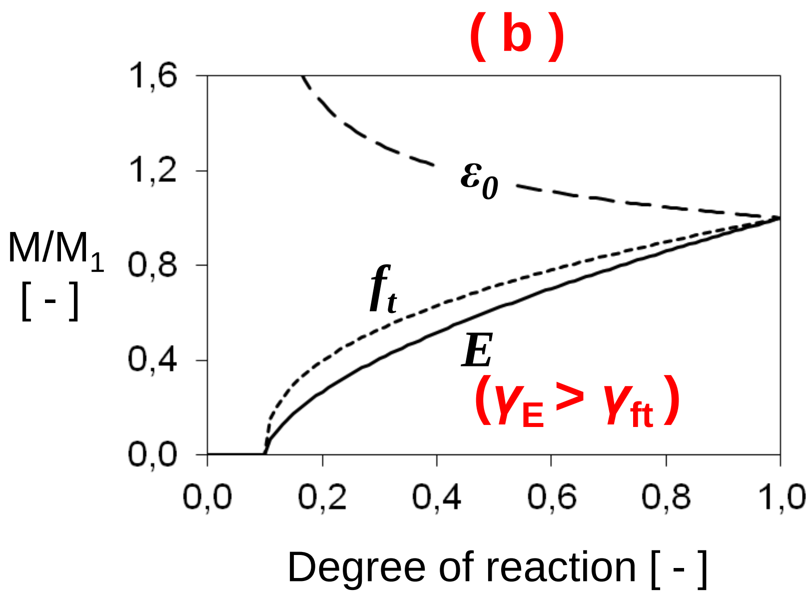
$$\alpha = 1 - K_T / K_S$$

Mechanical properties *vs* hydration degree

De Schutter type equation*:

$$\frac{M(\Gamma)}{M_1} = \left\langle \frac{\Gamma - \Gamma_0}{1 - \Gamma_0} \right\rangle_+^{\gamma_M}$$

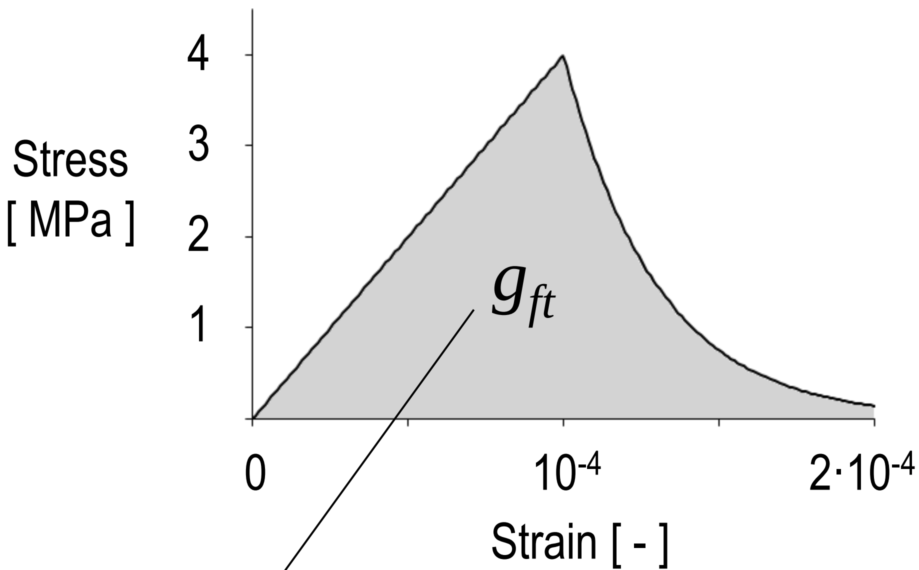




*This law is used for **Young's modulus**, **tensile strength** and **fracture energy.**

The damage model

Tensile branch of the t-e relationship (J. Mazars)



$$D = 1 - \frac{e_0}{\hat{e}} \exp\left[-B_t \left(\hat{e} - e_0 \right) \right]$$

Damage criterion: $f = \hat{e} - e_0$

with $\hat{e} = \sqrt{\langle e_{el} \rangle_+ : \langle e_{el} \rangle_+ + \psi \langle e_{cr} \rangle_+ : \langle e_{cr} \rangle_+}$

$$g_{ft} = \int_0^\infty t\,de = f_t \left(\frac{e_0}{2} + \frac{1}{B_t} \right) \qquad \left[\frac{\mathrm{N}}{\mathrm{m}^2} \right]$$

$$g_{ft} = \frac{G_{ft}}{l_c}$$

G_{ft} — fracture energy

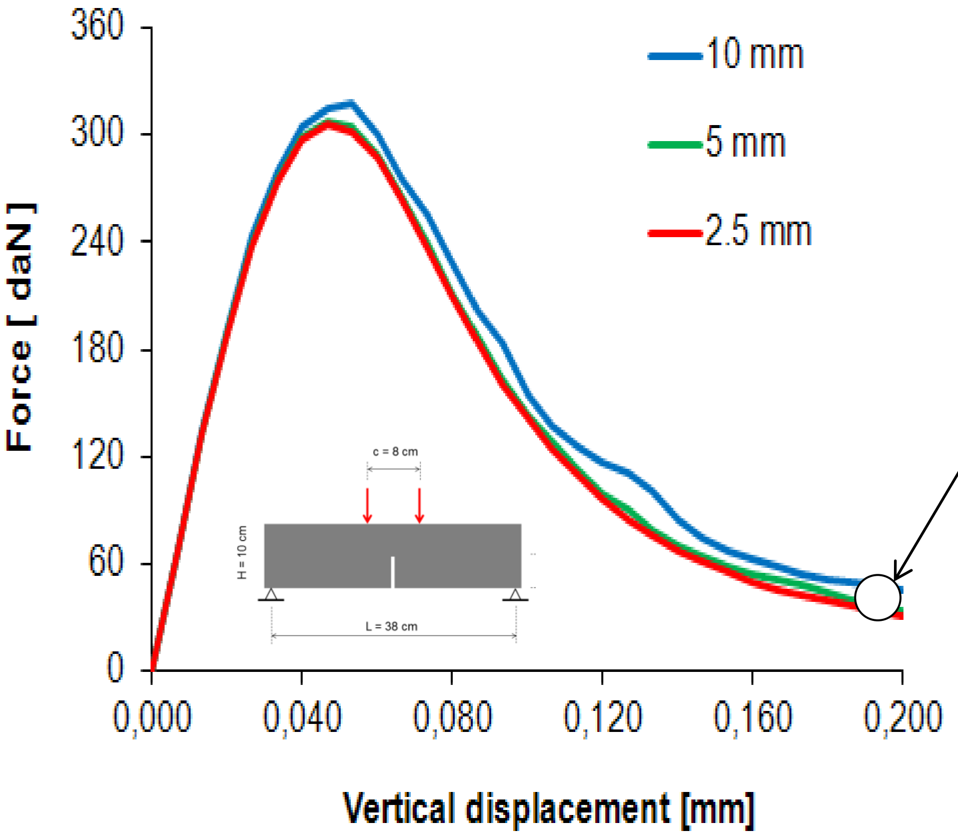
l_c — finite element characteristic length

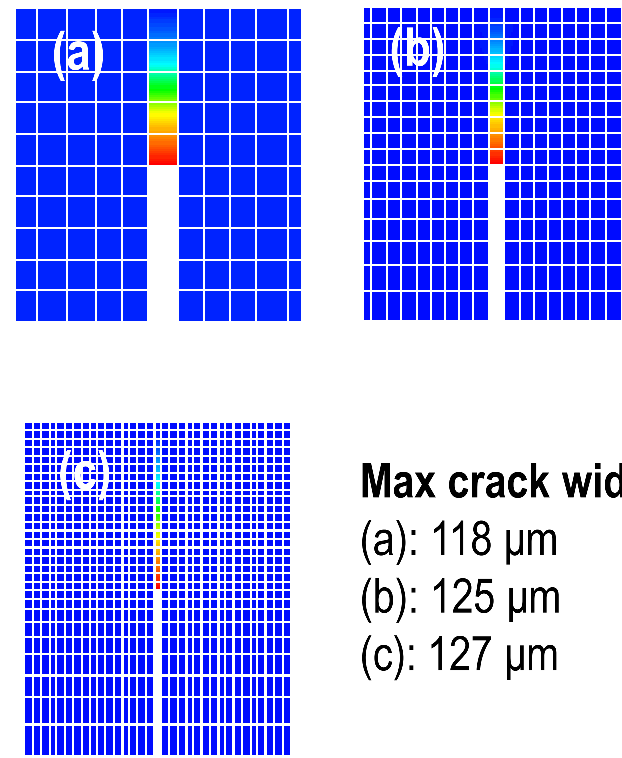
Regularization

$$B_t = \frac{f_t}{G_{ft} - \frac{f_t^2}{2E} l_c} l_c$$

The damage model

Four points bending test





Max crack width:

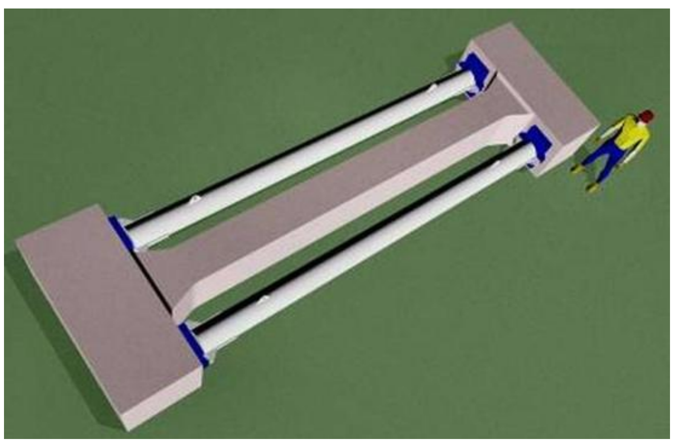
(a): 118 μm

(b): 125 μm

(c): 127 μm

ConCrack Benchmark*

ConCrack.org



RG8: Large specimen with restrained shrinkage

DESCRIPTION OF THE TEST

The longitudinal strains of the structure are globally restrained by two struts.

-During the first 2 days after the cast, the structure is isolated.

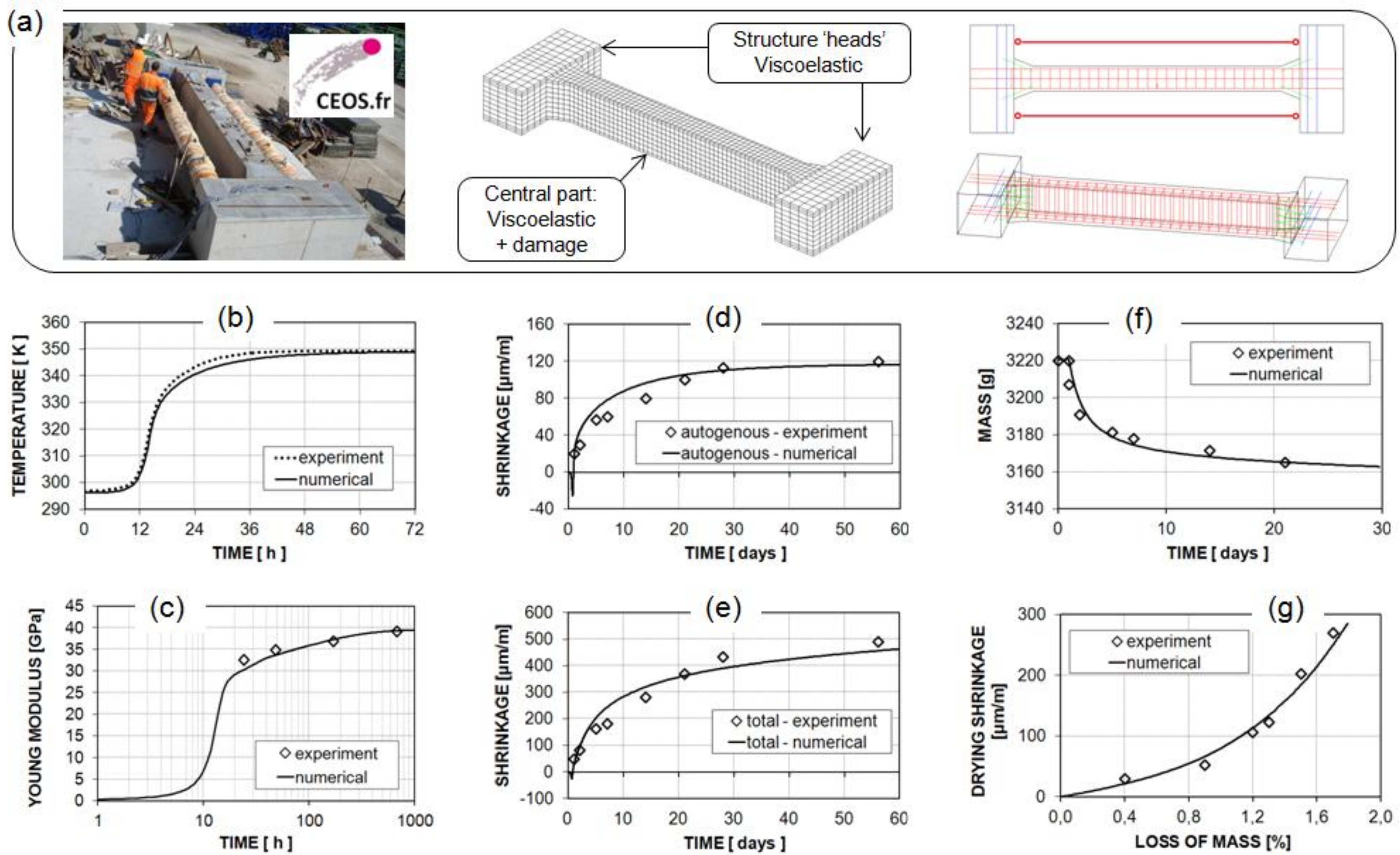
-Then the isolation and the formwork are removed and the structure is conserved during 2 months in the environment

-Therefore after this two months, the structure is submitted to a static bending test.

**ConCrack* (2011) is an international benchmark for Control of Cracking in reinforced concrete structures. This benchmark is part of the national French project CEOS (*Comportement et Evaluation des Ouvrages Speciaux vis-à-vis de la fissuration et du retrait*) dedicated to the analysis of the behaviour of special construction works concerning cracking and shrinkage.

CEOS.fr

ConCrack Benchmark

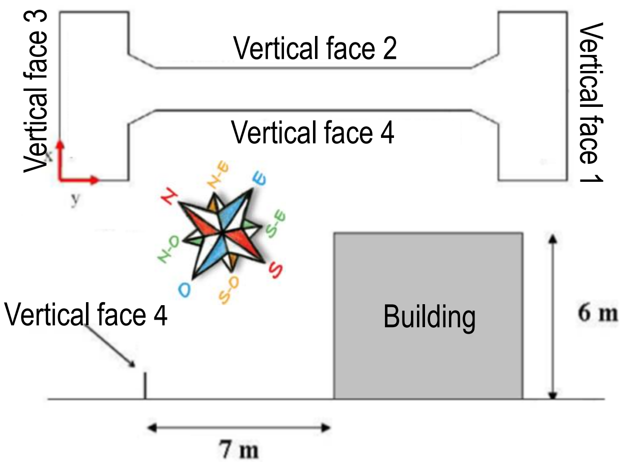


From the left to the right: image of the structure, finite element mesh of the concrete and of the reinforcement bars (a). Adiabatic calorimetry test (b). Evolution of the Young's modulus with time (c). Autogenous (d) and total (e) shrinkage tests. Loss of mass test (f). Loss of mass versus drying shrinkage (g).

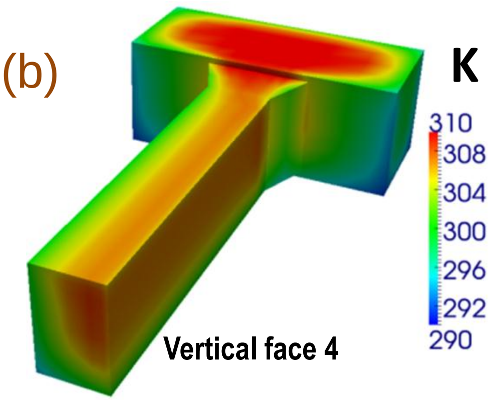
ConCrack Benchmark: THC results

TEMPERATURE

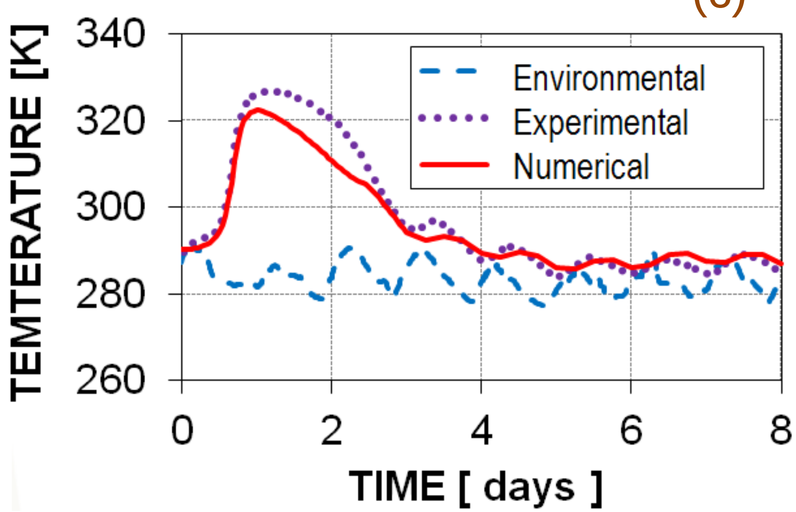
SOLAR RADIATION CONSIDERED



(a)



(b)

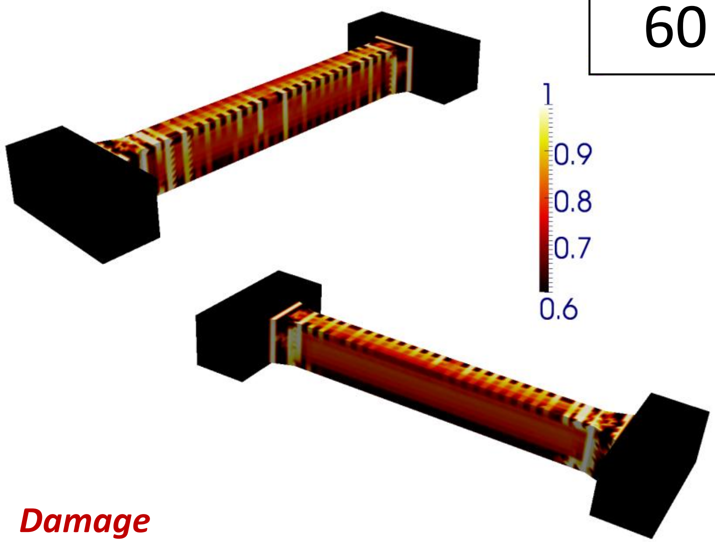


(c)

(a) Specimen orientation;
(b) Temperature 2,25 days after the cast (afternoon);
(c) Experimental and numerical results for the temperature in the central point of the beam.

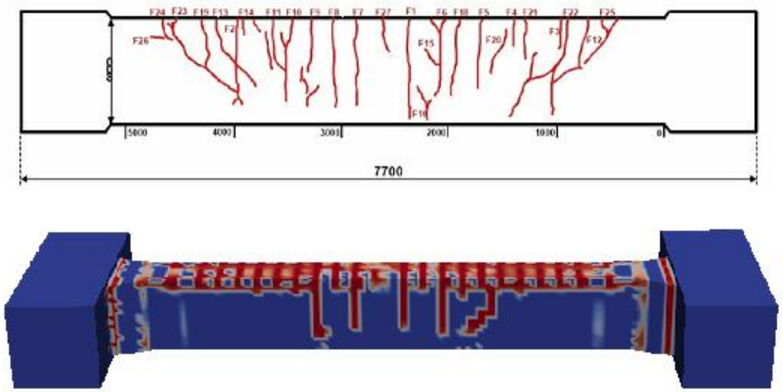
ConCrack Benchmark: MEC results

60 days

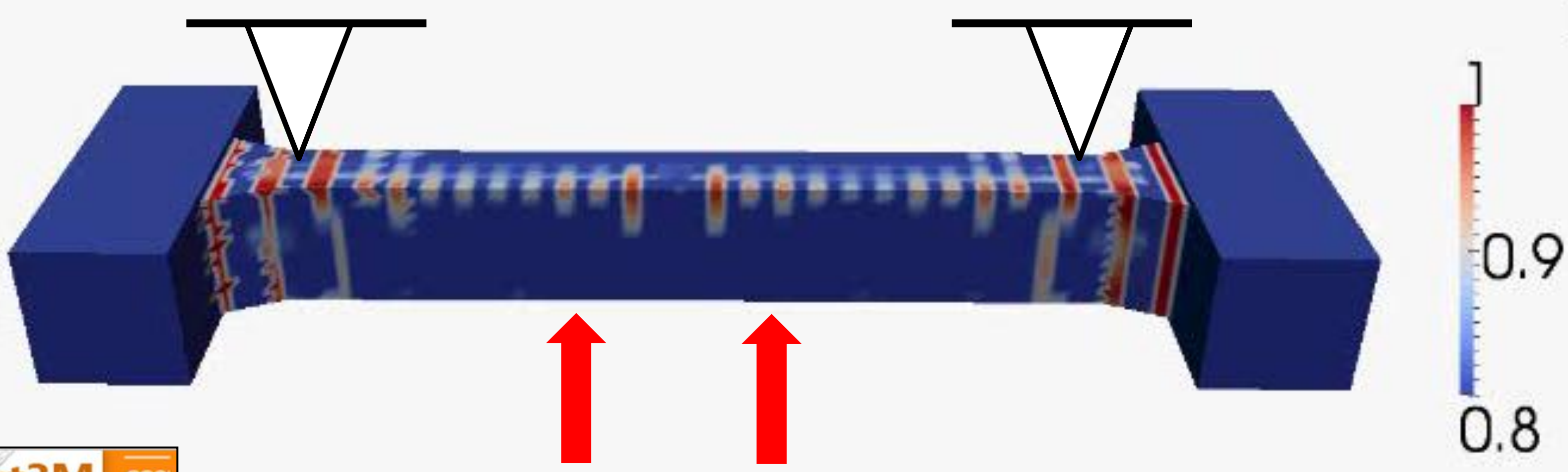


Damage

Four point bending test

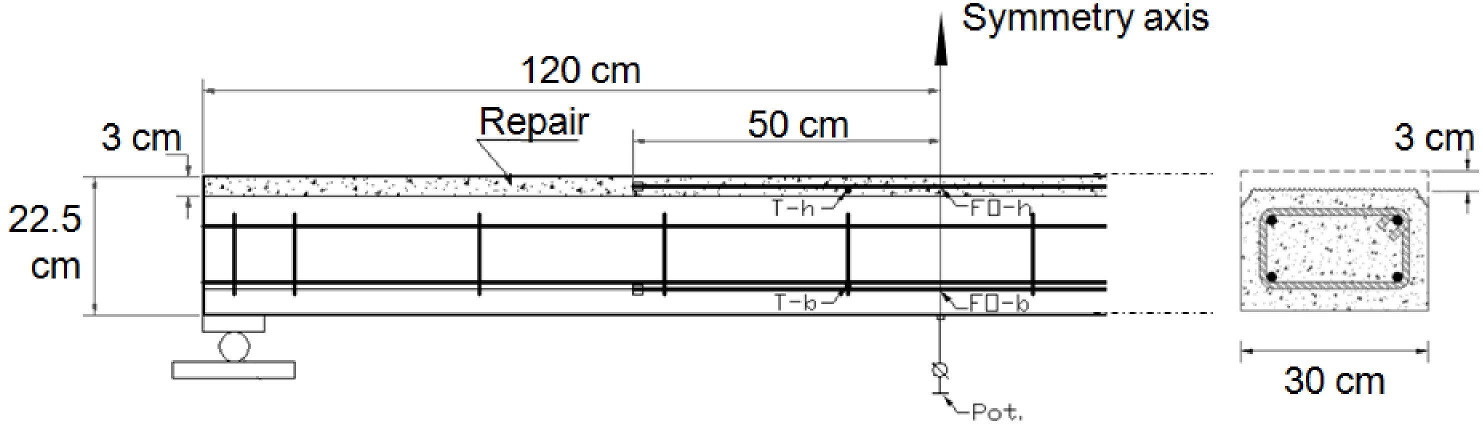


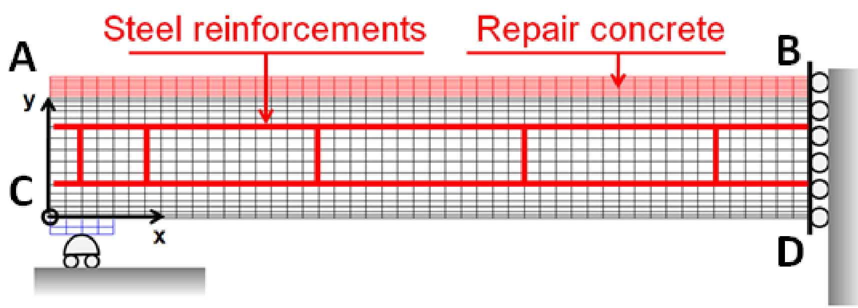
Cracks pattern



Cast3M cea

Modeling of a repaired beam





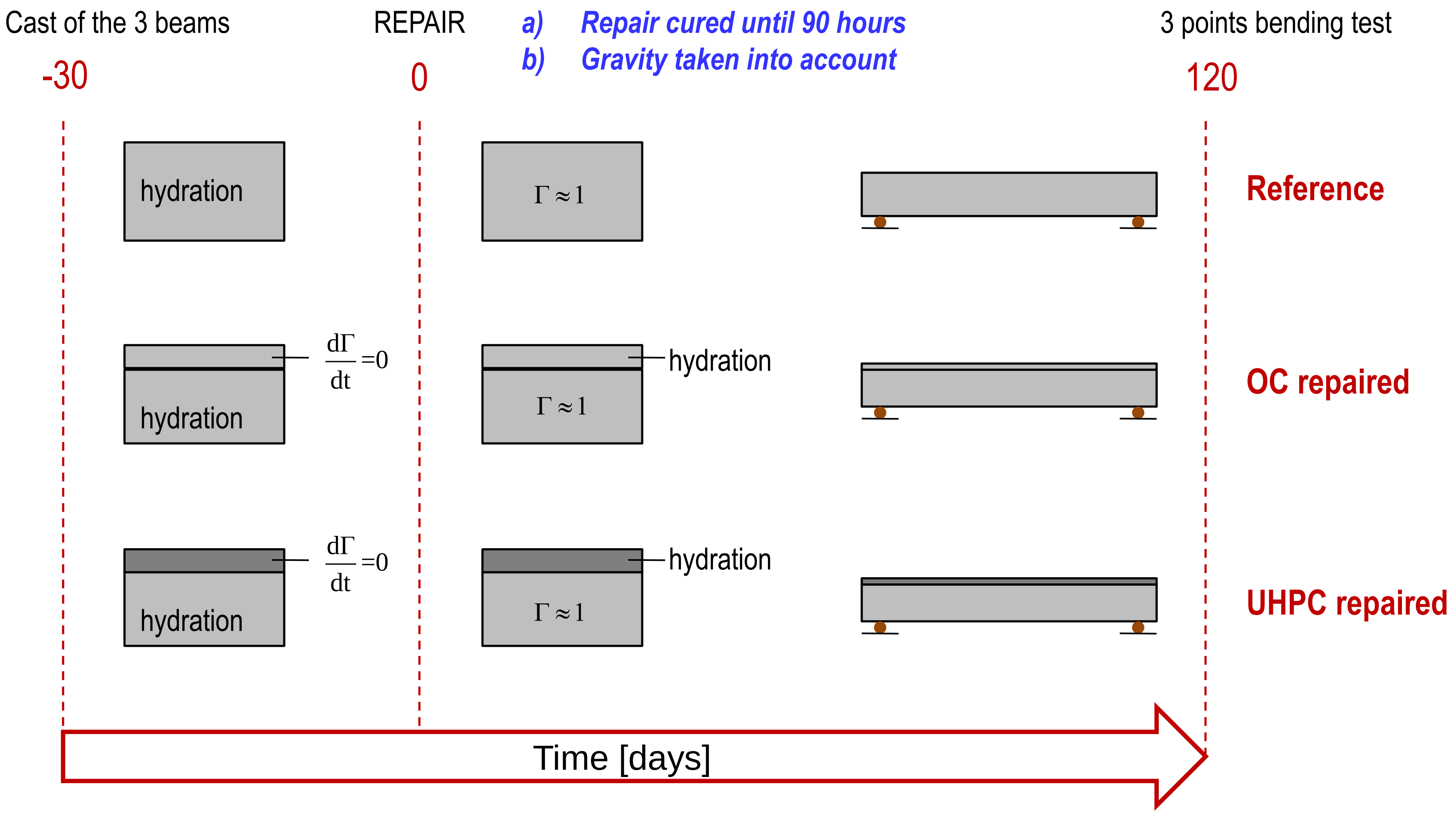
-T-b: lower thermocouple
-T-h: higher thermocouple
-Pot: linear potentiometer
-FO-b: lower fiber-optic sensor
-FO-h: higher fiber-optic sensor

Three identical reinforced beams* are considered. Two of these beams, after the hydrodemolition of 30 mm of the upper part, had been repaired: one using the **ordinary concrete (OC)** and the other using the **ultra-high performance fiber reinforced concrete (UHPC).** The third beam is the reference specimen.

***These repaired beams are real cases analyzed experimentally by Bastien Masse (2010**).

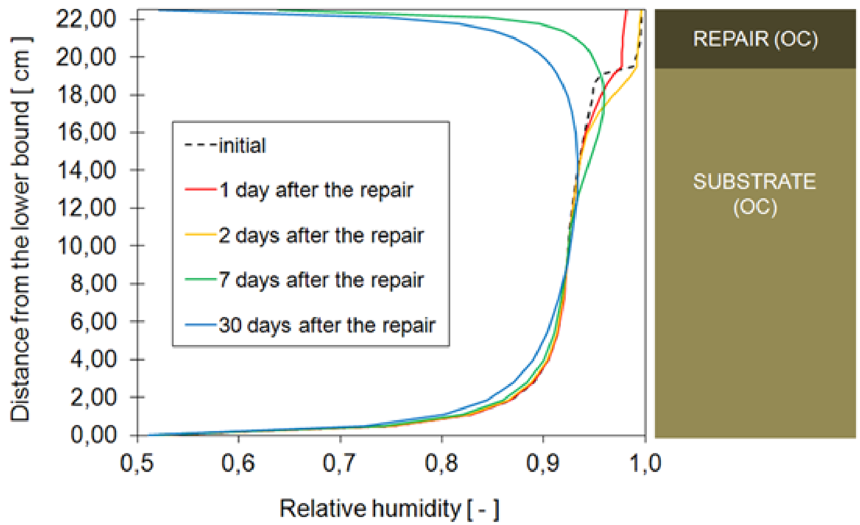
Modeling of a repaired beam

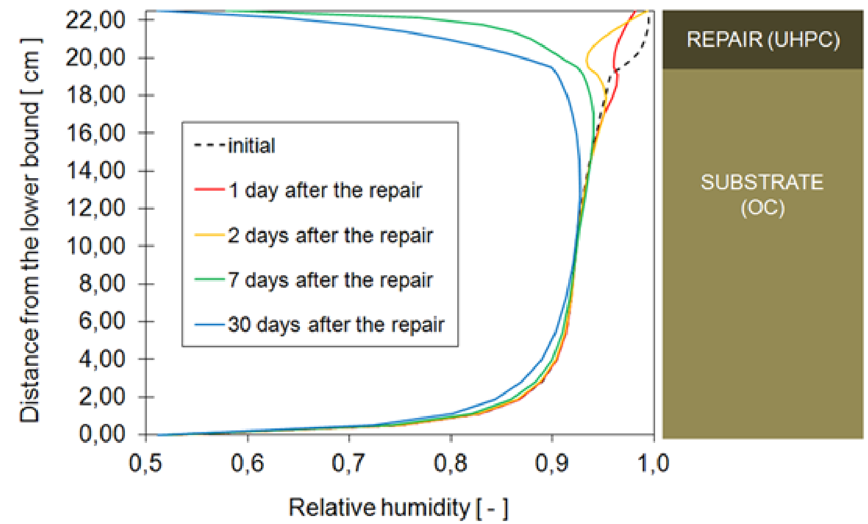
ADOPTED APPROACH

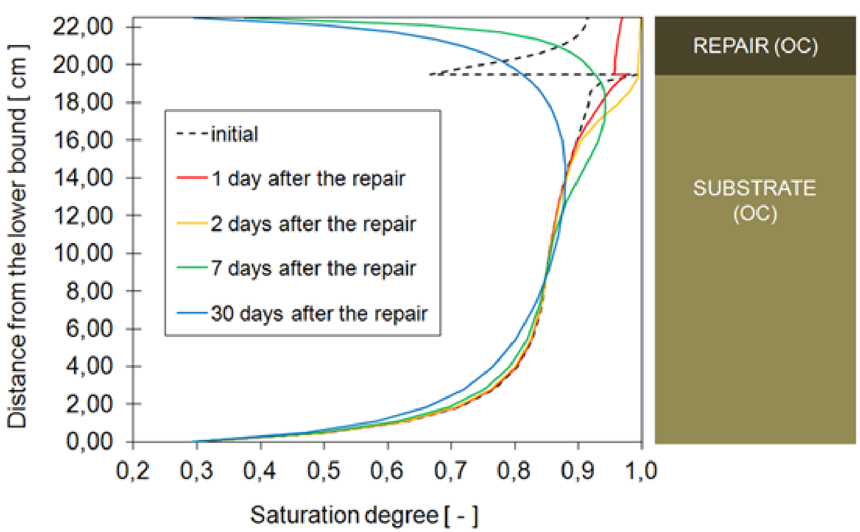


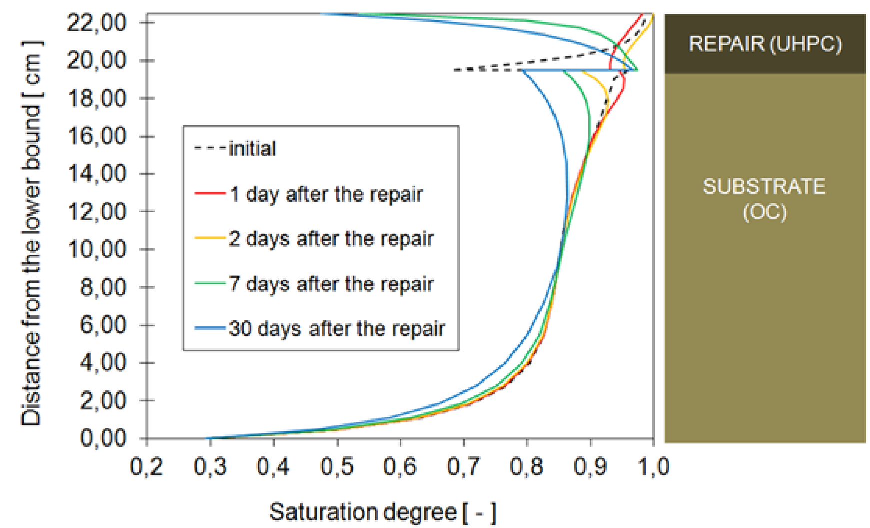
Modeling of a repaired beam

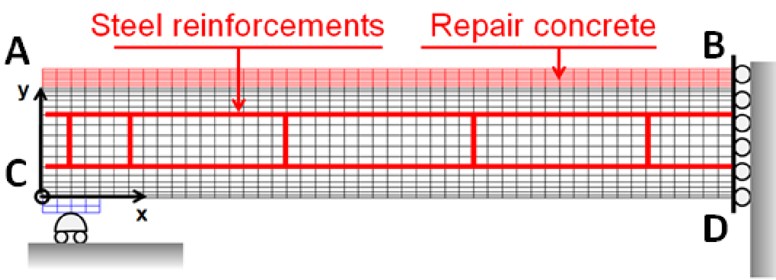
RELATIVE HUMIDITY AND SATURATION DEGREE



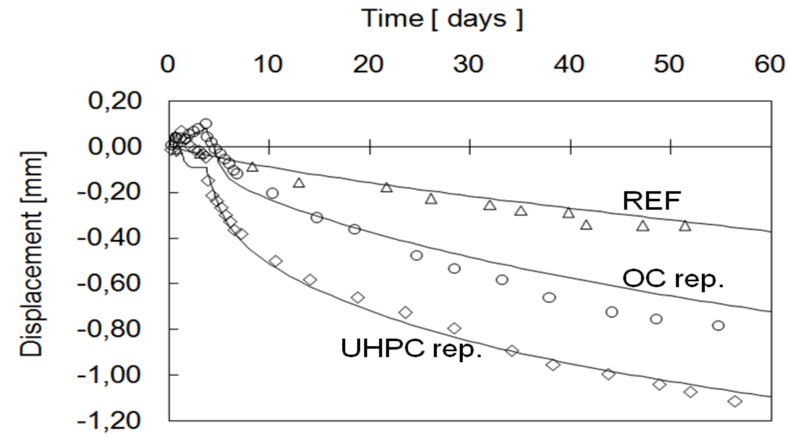




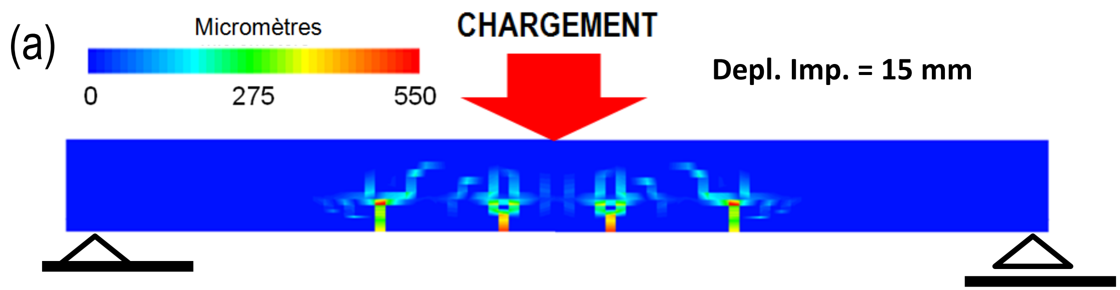




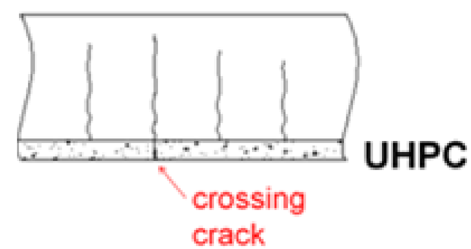
Vertical displacement of the middle points of the three beams (point D).



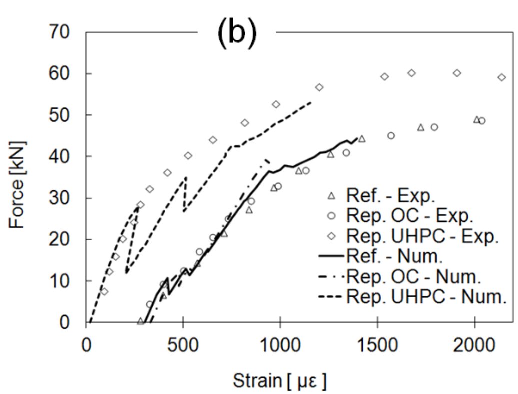
3-points bending test

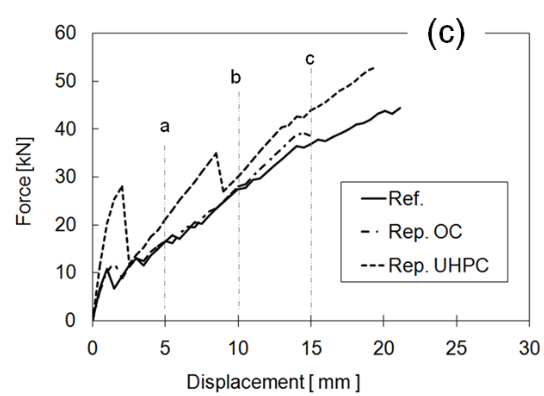


(a) Beam repaired using the UHPC. Only some racks are traversing



Experimental crack pattern





(b) Force versus averaged strain of the compressed fiber optic sensor.

(c) Force versus displacement curves (numerical results).

Concrete at early age

Tumor growth

- Outline of the general mathematical model
- Three applications of biological interest
- Recent advances and perspectives

General conclusions

Contributions and Acknowledgements

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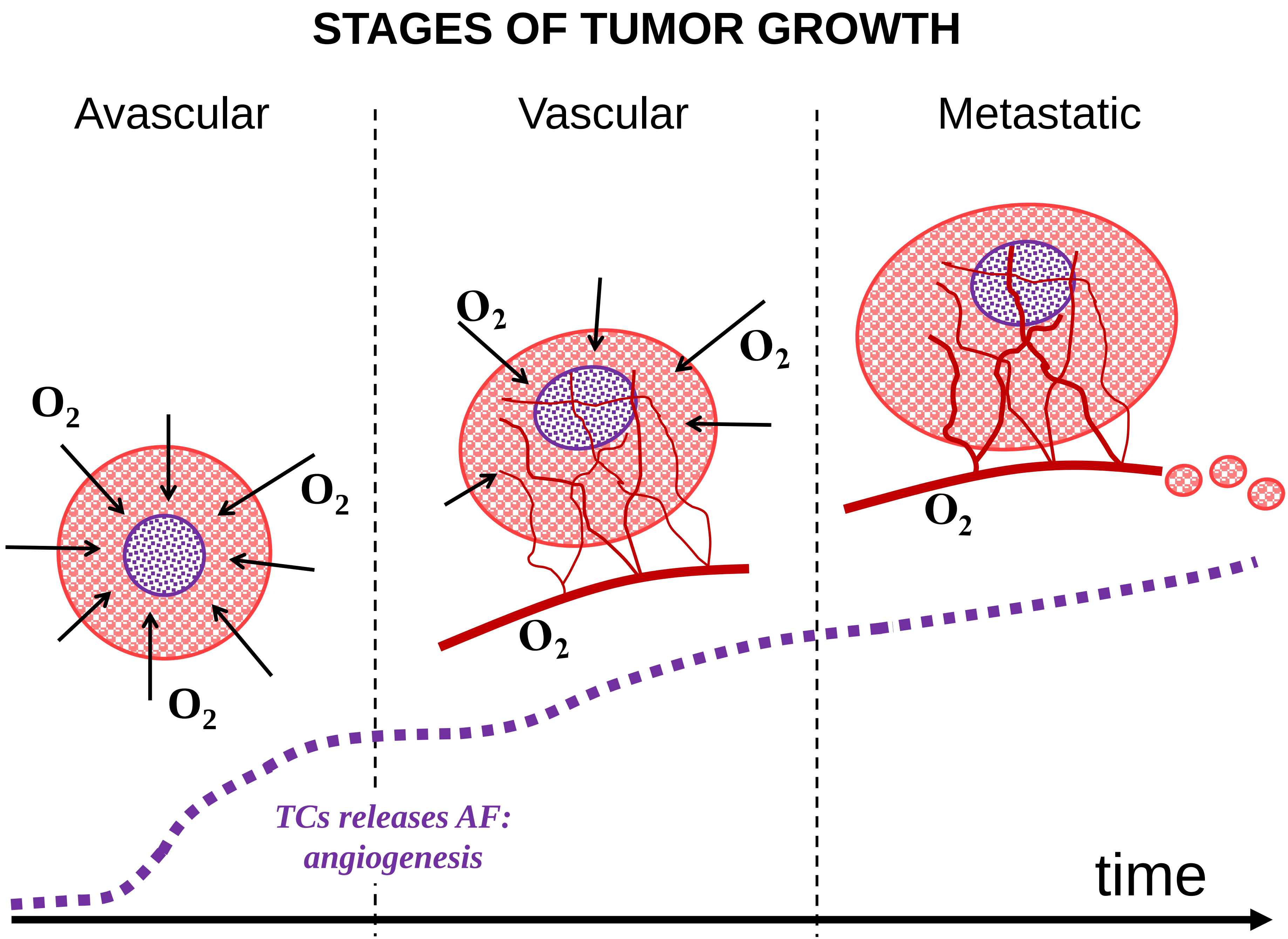
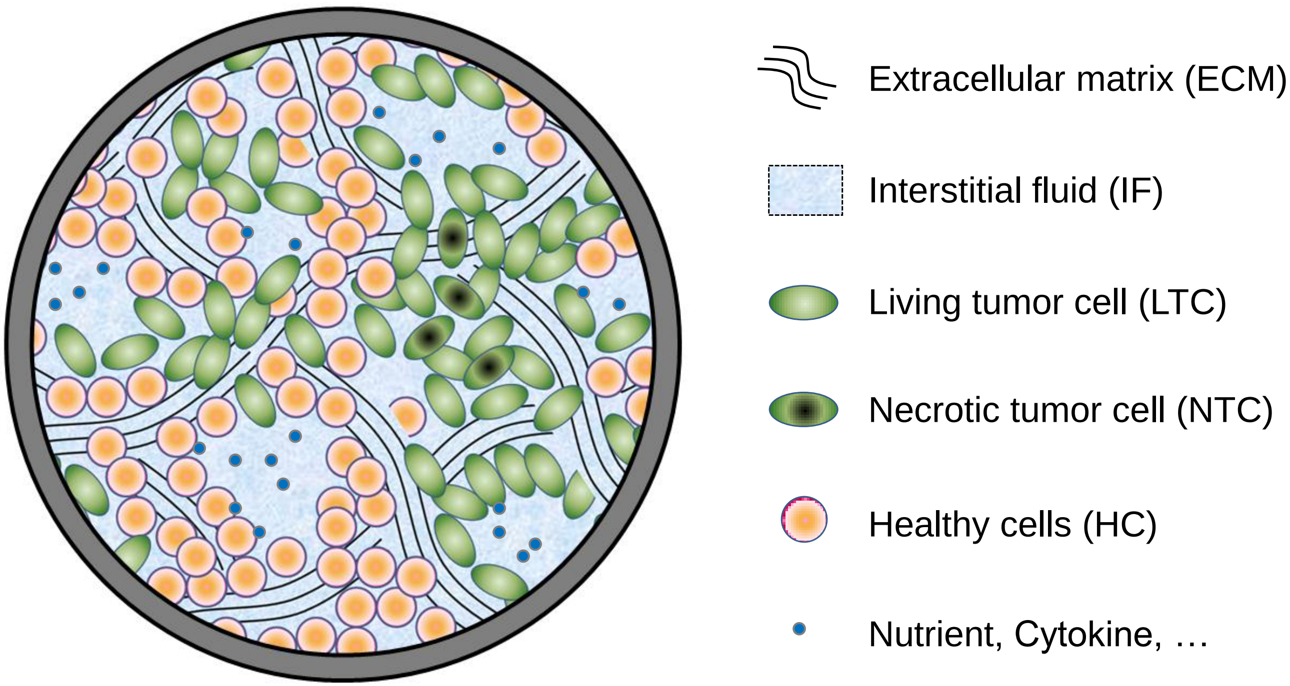

STAGES OF TUMOR GROWTH
Avascular
Vascular
Metastatic
O_2
O_2
O_2
O_2
O_2
O_2
O_2
TCs releases AF:
angiogenesis
time

The MULTI-PHASE system

FOR AVASCULAR TUMOR GROWTH

4 PHASES ARE CONSIDERED

The system consists of the extra-cellular matrix, **ECM**, modeled as a solid phase, and three immiscible fluid phases: the tumor cell population **TC**, the host cell population **HC**, and the interstitial fluid **IF**.



The MULTI-PHASE system

FOR AVASCULAR TUMOR GROWTH

We model IF, HC and TC as fluids: 3-phase flow with interfacial properties

Diffuse interface model: interfaces are present throughout the domain

Cell migration in a 3D extracellular matrix

Gabriel G. Martins and John Kolega (2006)

Surface tension of cell aggregates varies between $1x10^{-3}$ and $22x10^{-3}$ N/m

Ambrosi et al. 2012

Surface tension of water $72x10^{-3}$ N/m

Volume fractions

Volume fractions occupied by the different phases:

$$\varepsilon^s + \varepsilon^h + \varepsilon^t + \varepsilon^l = 1$$

Extra-cellular matrix

Host cells

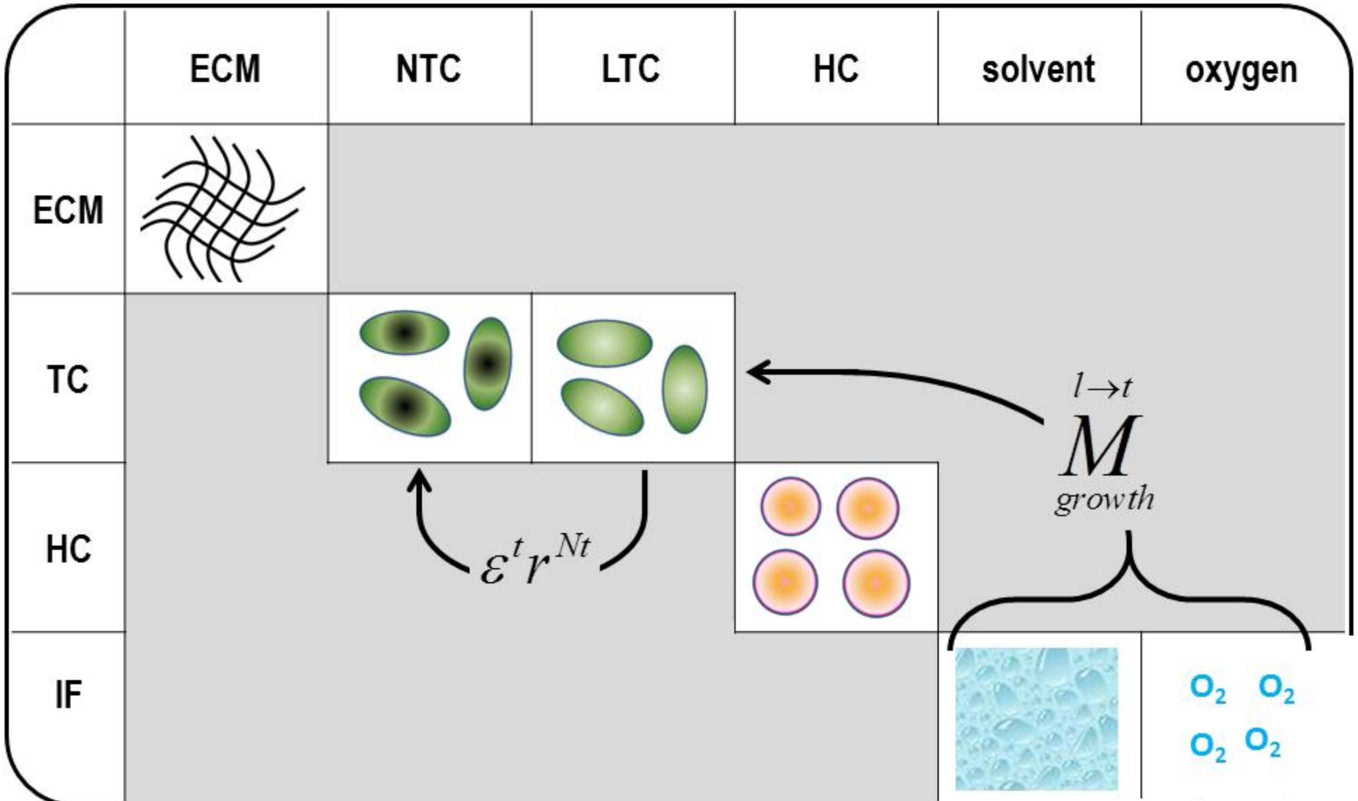
Tumor cells

Interstitial fluid

Model derivation and its solution

- Mass balance equations of phases and species;
- Linear momentum balance equations of phases;
- Constitutive relationships to close the model;
- Numerical solution and computational strategy.

Mass exchanges $\overset{\alpha\rightarrow\beta}{M}$ and reaction terms $\varepsilon^s r^{Hs}$



Co-opted blood vessels considered
via boundary conditions

Mass balance eqs of phases and species

$$\text{IF}\,[\,l\,]:\quad \frac{\partial\left(\rho^{l}\varepsilon S^{l}\right)}{\partial t}+\nabla\cdot\left(\rho^{l}\varepsilon S^{l}\mathbf{v}^{l}\right)+\overset{l\rightarrow t}{\underset{growth}{M}}=0$$

Summing over all species gives

Mass balance of species *i* in *IF*

$$\frac{\partial\left(\varepsilon^{l}\rho^{l}\omega^{\bar{i}l}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^{l}\rho^{l}\omega^{\bar{i}l}\mathbf{v}^{\bar{l}}\right)+\nabla\cdot\left(\varepsilon^{l}\rho^{l}\omega^{\bar{i}l}\mathbf{u}^{\bar{\bar{i}}l}\right)+\overset{il\rightarrow it}{M}=0$$

Mass balance eqs of phases and species

LTC : $$\frac{\partial\left[\varepsilon^t\rho^t\left(1-\omega^{N\bar{t}}\right)\right]}{\partial t}+\nabla\cdot\left[\varepsilon^t\rho^t\left(1-\omega^{N\bar{t}}\right)\mathbf{v}^{\bar{t}}\right]+\varepsilon^t r^{Nt}-\overset{l\rightarrow t}{M}=0$$

NTC : $$\frac{\partial\left(\varepsilon^t\rho^t\omega^{N\bar{t}}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^t\rho^t\omega^{N\bar{t}}\mathbf{v}^{\bar{t}}\right)-\varepsilon^t r^{Nt}=0$$

Summing these two eqs gives

Ts [*t*] : $$\frac{\partial\left(\rho^t\varepsilon S^t\right)}{\partial t}+\nabla\cdot\left[\rho^t\varepsilon S^t\mathbf{v}^t\right]-\underset{growth}{\overset{l\rightarrow t}{M}}=0$$

IF [*l*] : $$\frac{\partial\left(\rho^l\varepsilon S^l\right)}{\partial t}+\nabla\cdot\left(\rho^l\varepsilon S^l\mathbf{v}^l\right)+\underset{growth}{\overset{l\rightarrow t}{M}}=0$$

Summing over all species gives

Mass balance of species *i* in *IF*

$$\frac{\partial\left(\varepsilon^l\rho^l\omega^{\bar{il}}\right)}{\partial t}+\nabla\cdot\left(\varepsilon^l\rho^l\omega^{\bar{il}}\mathbf{v}^{\bar{l}}\right)+\nabla\cdot\left(\varepsilon^l\rho^l\omega^{\bar{il}}\mathbf{u}^{\bar{\bar{il}}}\right)+\overset{il\rightarrow it}{M}=0$$

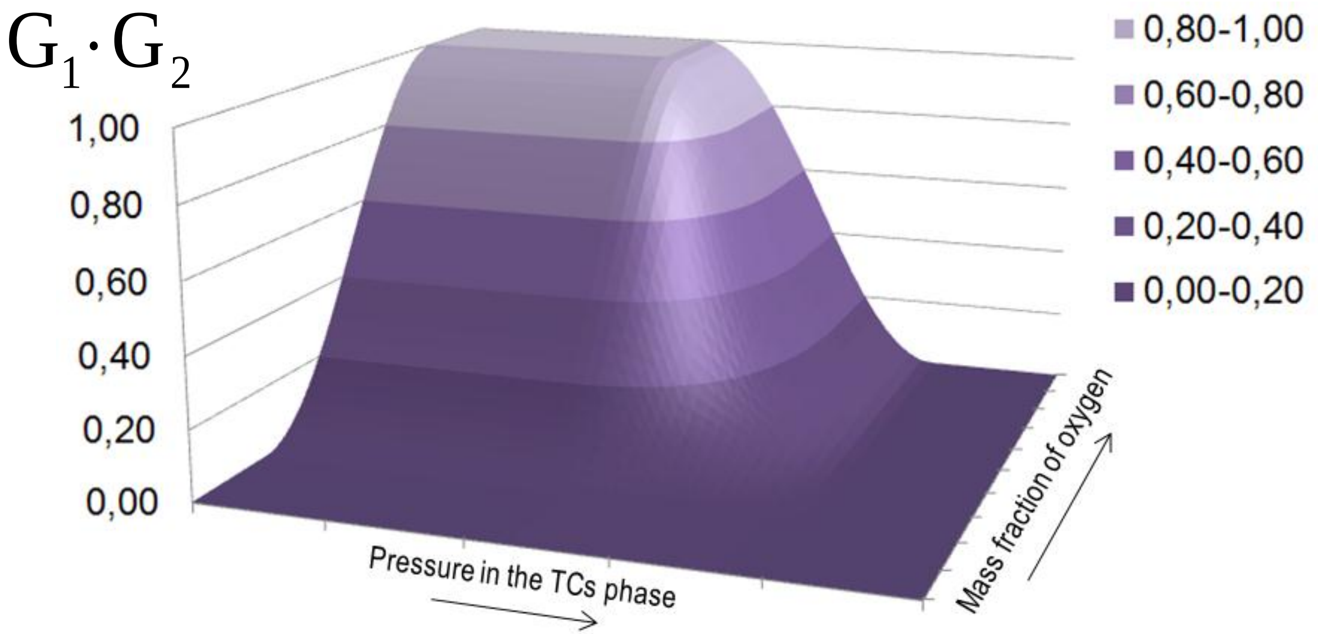
Mass balance eqs of phases and species

$$
\begin{cases}
\text{ECM} [\, s \,] : & \dfrac{\partial\left[\rho^{s}(1-\varepsilon)\right]}{\partial t} + \nabla\cdot\left[\rho^{s}(1-\varepsilon)\mathbf{v}^{s}\right] = 0 \\[2ex]
\text{HCs} [\, h \,] : & \dfrac{\partial\left[\rho^{h}\varepsilon S^{h}\right]}{\partial t} + \nabla\cdot\left[\rho^{h}\varepsilon S^{h}\mathbf{v}^{h}\right] = 0 \\[2ex]
\text{TCs} [\, t \,] : & \dfrac{\partial\left(\rho^{t}\varepsilon S^{t}\right)}{\partial t} + \nabla\cdot\left[\rho^{t}\varepsilon S^{t}\mathbf{v}^{t}\right] - \overset{l\rightarrow t}{\underset{growth}{M}} = 0 \\[2ex]
\text{IF} [\, l \,] : & \dfrac{\partial\left(\rho^{l}\varepsilon S^{l}\right)}{\partial t} + \nabla\cdot\left(\rho^{l}\varepsilon S^{l}\mathbf{v}^{l}\right) + \overset{l\rightarrow t}{\underset{growth}{M}} = 0 \\[2ex]
\text{Oxy} [\, n \,] : & \dfrac{\partial\left(\varepsilon^{l}\rho^{l}\omega^{\overline{nl}}\right)}{\partial t} + \nabla\cdot\left(\varepsilon^{l}\rho^{l}\omega^{\overline{nl}}\mathbf{v}^{\bar{l}}\right) + \nabla\cdot\left(\varepsilon^{l}\rho^{l}\omega^{\overline{nl}}\mathbf{u}^{\overline{\overline{nl}}}\right) + \overset{n\rightarrow t}{M} = 0
\end{cases}
$$

Mass balance eqs of phases and species

TCs [*t*] :

$$\frac{\partial\left(\rho^t \varepsilon S^t\right)}{\partial t} + \nabla \cdot \left[\rho^t \varepsilon S^t \mathbf{v}^t\right] - \overset{l \to t}{\underset{growth}{M}} = 0$$

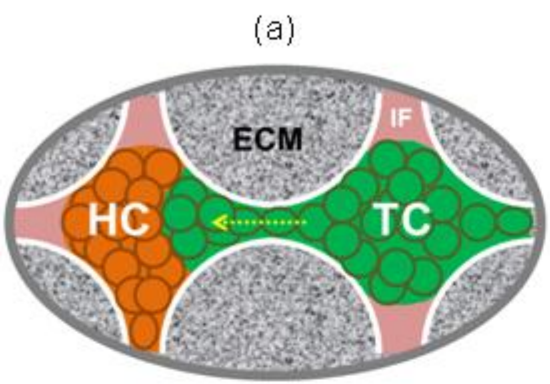


$$\overset{l \to t}{\underset{growth}{M}} = \sum_{i \in l} \overset{il \to it}{M} = \left[\gamma^t_{growth}\, \mathrm{G}_1\left(\omega^{\overline{nl}}\right) \mathrm{G}_2\left(p^t\right)\right]\left(1 - \omega^{\bar{N}t}\right) \varepsilon S^t$$

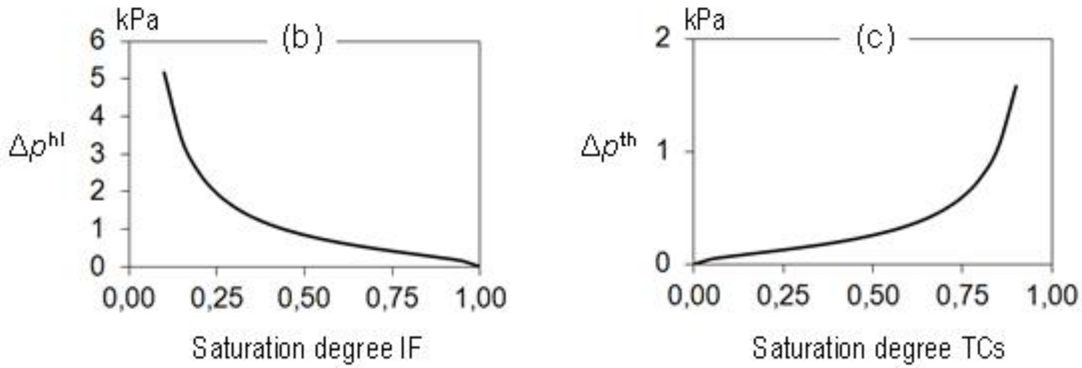
Pressure saturation relationships

Interfaces are capable to sustain a pressure difference

Each of the three fluids of the multiphase system has its specific pressure, p^α, so a pressure difference exists between any pair of fluid phases:



$$p^{hl} = p^h - p^l$$
$$p^{th} = p^t - p^h$$
$$p^{tl} = p^t - p^l = p^{th} + p^{hl}$$



$$p^{hl}\left(S^l\right) = a \tan\left[\frac{\pi}{2}\left(1 - S^l\right)^b\right]$$

$$p^{th}\left(S^t\right) = a \frac{\sigma_{th}}{\sigma_{hl}} \tan\left[\frac{\pi}{2}\left(S^t\right)^b\right]$$

Interfacial tensions appear explicitly

Fluid phases configuration and flows of cells within ECM micro-channels (a).
Pressure difference - saturation relationships (b, c)

Final system of eqs

Primary variables

$$p^{th} \quad p^{hl} \quad p^{l} \quad \omega^{\overline{nl}} \quad \mathbf{u}_s$$

Mass balance eqn OXYGEN

$$\varepsilon S^l \frac{\partial \omega^{\overline{nl}}}{\partial t} - \nabla \cdot \left(\varepsilon S^l D_{eff}^{\overline{nl}} \nabla \omega^{\overline{nl}} \right) = \frac{1}{\rho^l} \left(\omega^{\overline{nl}} \overset{l \to t}{M} - \overset{nl \to t}{M} \right) - \varepsilon S^l \mathbf{v}^{\bar{l}} \cdot \nabla \omega^{\overline{nl}}$$

Mass balance eqn TC

$$\left[\frac{\varepsilon S^t}{K_T} + \frac{S^t (1-\varepsilon)}{K_S} \left(S^t + p^{th} \frac{\partial S^t}{\partial p^{th}} \right) + \varepsilon \frac{\partial S^t}{\partial p^{th}} \right] \frac{\partial p^{th}}{\partial t} + \left[\frac{\varepsilon S^t}{K_T} + \frac{S^t (1-\varepsilon)}{K_S} \left(1 - S^l - p^{hl} \frac{\partial S^l}{\partial p^{hl}} \right) \right] \frac{\partial p^{hl}}{\partial t} +$$

$$+ \left[\frac{\varepsilon S^t}{K_T} + \frac{S^t (1-\varepsilon)}{K_S} \right] \frac{\partial p^l}{\partial t} = \nabla \cdot \left[\frac{k_{rel}^t \mathbf{k}}{\mu^t} \cdot \nabla \left(p^l + p^{hl} + p^{th} \right) \right] - S^t \left(\mathbf{1} : \mathbf{d}^{\bar{\bar{s}}} \right) - \nabla S^t \cdot \left(\varepsilon \mathbf{v}^{\bar{s}} \right) + \frac{1}{\rho^t} \overset{l \to t}{M}$$

Mass balance eqn HC

$$\left[\frac{S^h (1-\varepsilon)}{K_S} \left(S^t + p^{th} \frac{\partial S^t}{\partial p^{th}} \right) - \varepsilon \frac{\partial S^t}{\partial p^{th}} \right] \frac{\partial p^{th}}{\partial S^t} + \left[\frac{\varepsilon S^h}{K_H} + \frac{S^h (1-\varepsilon)}{K_S} \left(1 - S^l - p^{hl} \frac{\partial S^l}{\partial p^{hl}} \right) - \varepsilon \frac{\partial S^l}{\partial p^{hl}} \right] \frac{\partial p^{hl}}{\partial S^h} +$$

$$+ \left[\frac{\varepsilon S^h}{K_H} + \frac{S^h (1-\varepsilon)}{K_S} \right] \frac{\partial p^l}{\partial t} = \nabla \cdot \left(\frac{k_{rel}^h \mathbf{k}}{\mu^h} \cdot \nabla \left(p^l + p^{hl} \right) \right) - S^h \left(\mathbf{1} : \mathbf{d}^{\bar{\bar{s}}} \right) - \nabla S^h \cdot \left(\varepsilon \mathbf{v}^{\bar{s}} \right)$$

Mass balance eqn (TC + HC + IF)

$$\left[\frac{\varepsilon S^t}{K_T} + \frac{1-\varepsilon}{K_S} \left(S^t + p^{th} \frac{\partial S^t}{\partial p^{th}} \right) \right] \frac{\partial p^{th}}{\partial t} + \left[\frac{\varepsilon S^t}{K_T} + \frac{\varepsilon S^h}{K_H} + \frac{1-\varepsilon}{K_S} \left(1 - S^l - p^{hl} \frac{\partial S^l}{\partial p^{hl}} \right) \right] \frac{\partial p^{hl}}{\partial t} + \left(\frac{\varepsilon S^t}{K_T} + \frac{\varepsilon S^h}{K_H} + \frac{\varepsilon S^l}{K_L} + \frac{1-\varepsilon}{K_S} \right) \frac{\partial p^l}{\partial t} =$$

$$= \nabla \cdot \left[\frac{k_{rel}^t \mathbf{k}}{\mu^t} \cdot \nabla p^{th} \right] + \nabla \cdot \left[\left(\frac{k_{rel}^t \mathbf{k}}{\mu^t} + \frac{k_{rel}^h \mathbf{k}}{\mu^h} \right) \cdot \nabla p^{hl} \right] + \nabla \cdot \left[\left(\frac{k_{rel}^t \mathbf{k}}{\mu^t} + \frac{k_{rel}^h \mathbf{k}}{\mu^h} + \frac{k_{rel}^l \mathbf{k}}{\mu^l} \right) \cdot \nabla p^l \right] - \left(\mathbf{1} : \mathbf{d}^{\bar{\bar{s}}} \right) + \frac{\rho^l - \rho^t}{\rho^t \rho^l} \overset{l \to t}{M}$$

Linear momentum balance eqn ECM (rate form)

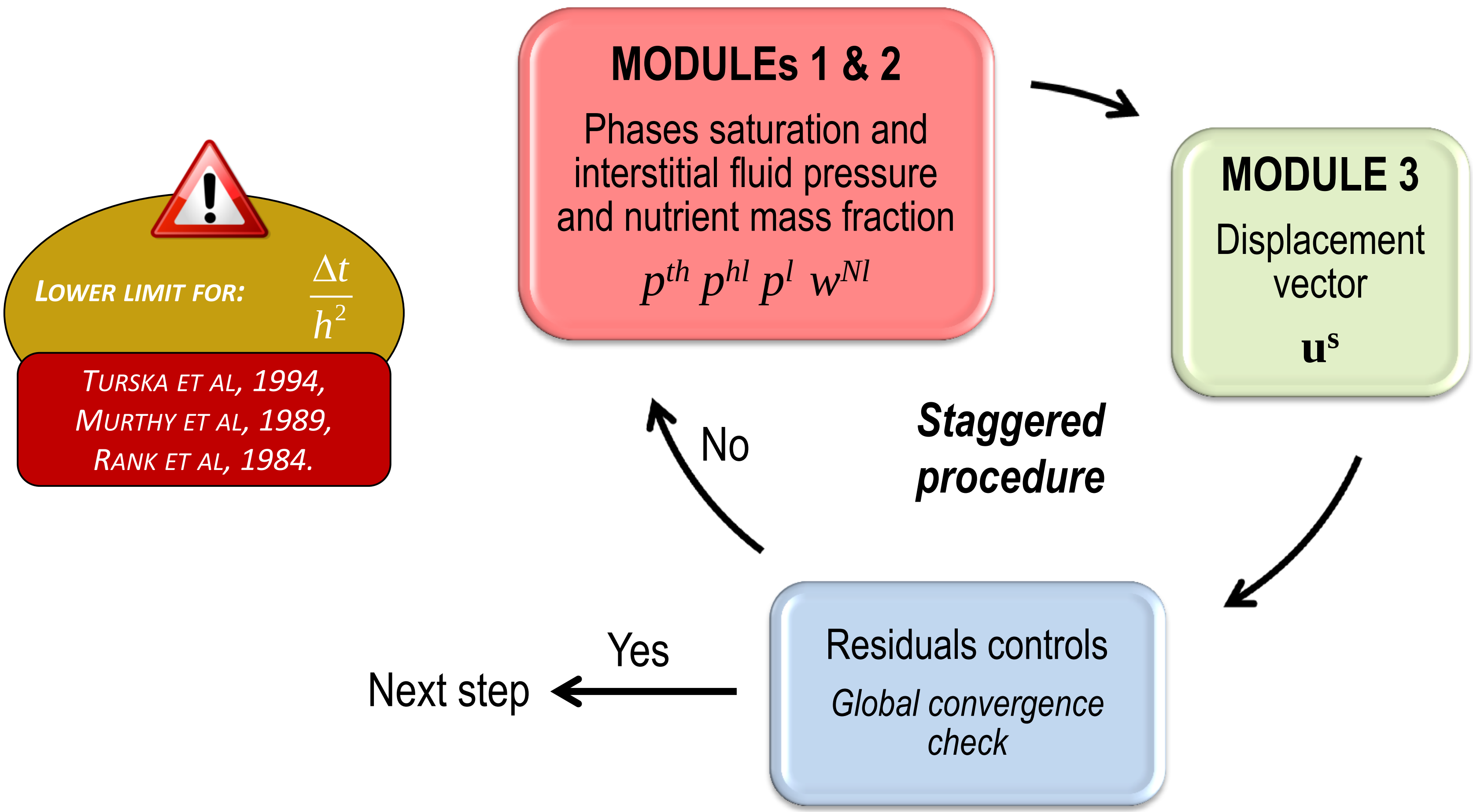
$$\nabla \cdot \left(\frac{\partial \mathbf{t}_{eff}^{\bar{\bar{s}}}}{\partial t} - \bar{\alpha} \frac{\partial p^s}{\partial t} \mathbf{1} \right) = 0$$

Numerical solution

Computational procedure

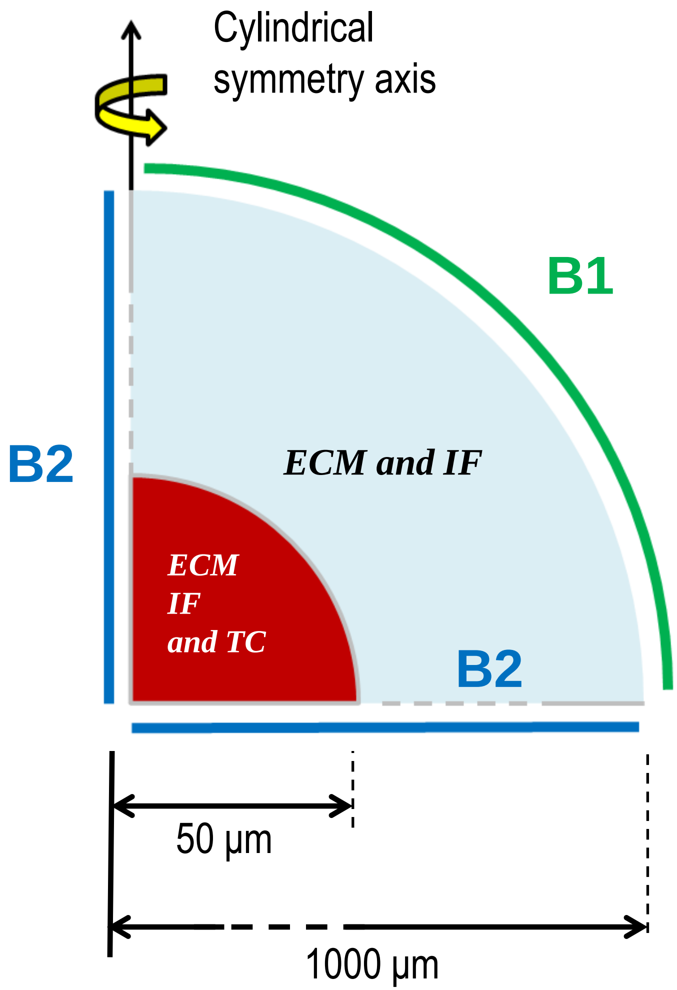
Primary variables

p^{th} p^{hl} p^{l} $\omega^{\overline{nl}}$ $\mathbf{u}_s$



CASE 1: MTS *IN VITRO*

The evolution of a multicellular tumor spheroid (MTS) in a quiescent, cell culture medium is modelled.



Boundary 1

Type: Imposed values

$\omega^{\overline{nl}} = \omega^{\overline{nl}}_{env} = 7.0 \cdot 10^{-6}$ $\quad \varepsilon^s = 1 - \varepsilon = 0.05$

$\varepsilon^h = \varepsilon S^h = 0.00$ $\quad \varepsilon^t = \varepsilon S^t = 0.00$

$p^l = 0\ mmHg$

Boundary 2

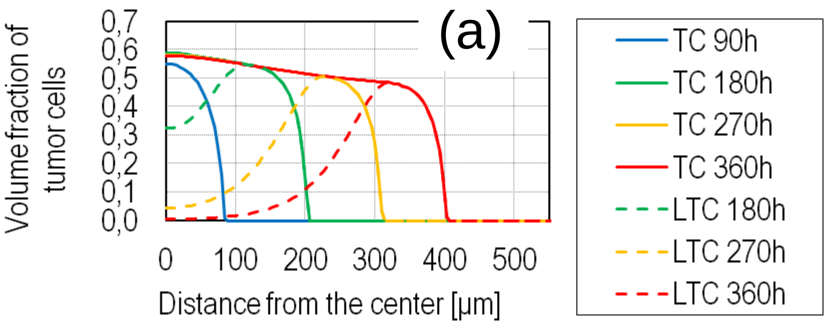
Type: Imposed fluxes

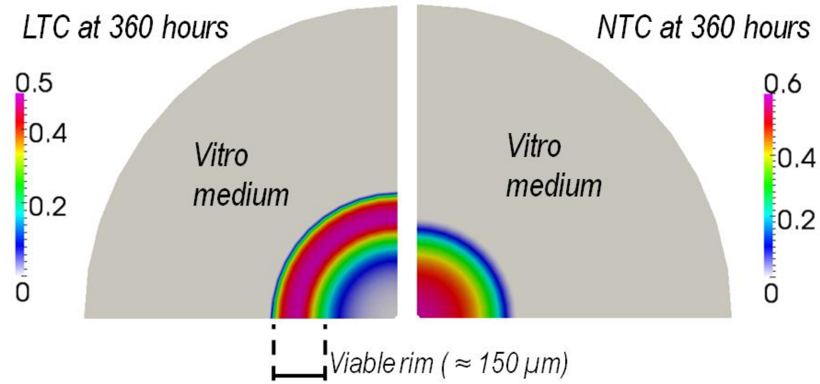
Due to the symmetry of the problem there are no normal fluxes.

Initial conditions:

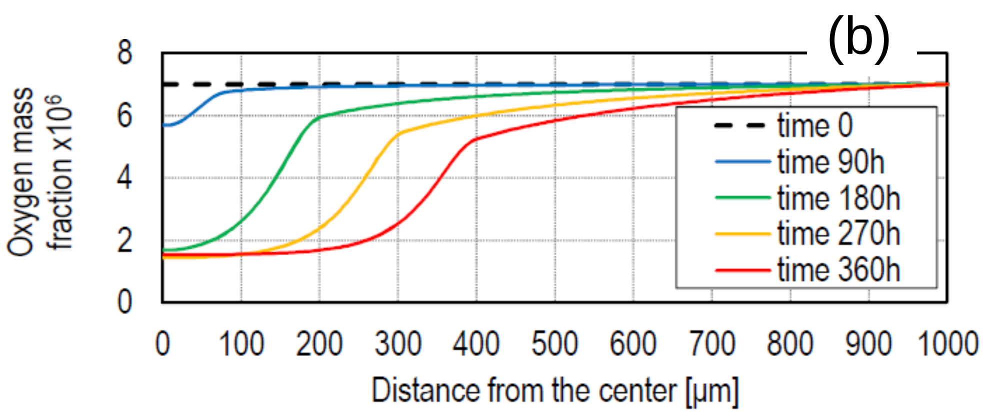
	ε^s	ε^t	ε^h	p^l	$\omega^{\overline{nl}}$
Red zone	0.05	0.01	0.00	0.00	$7 \cdot 10^{-6}$
Blu zone	0.05	0.00	0.00	0.00	$7 \cdot 10^{-6}$

CASE 1: MTS *IN VITRO*

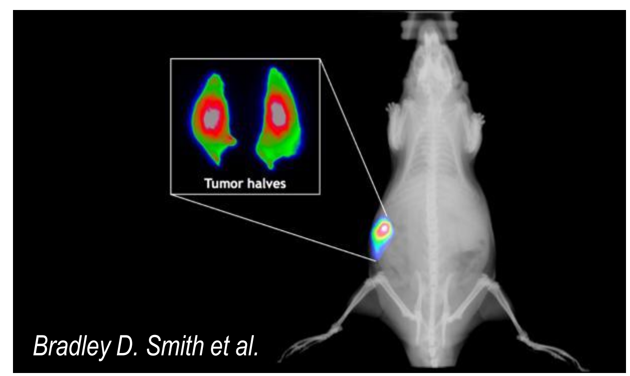




Living tumor cells (LTC) and necrotic tumor cells (NTC) at 360 hours.

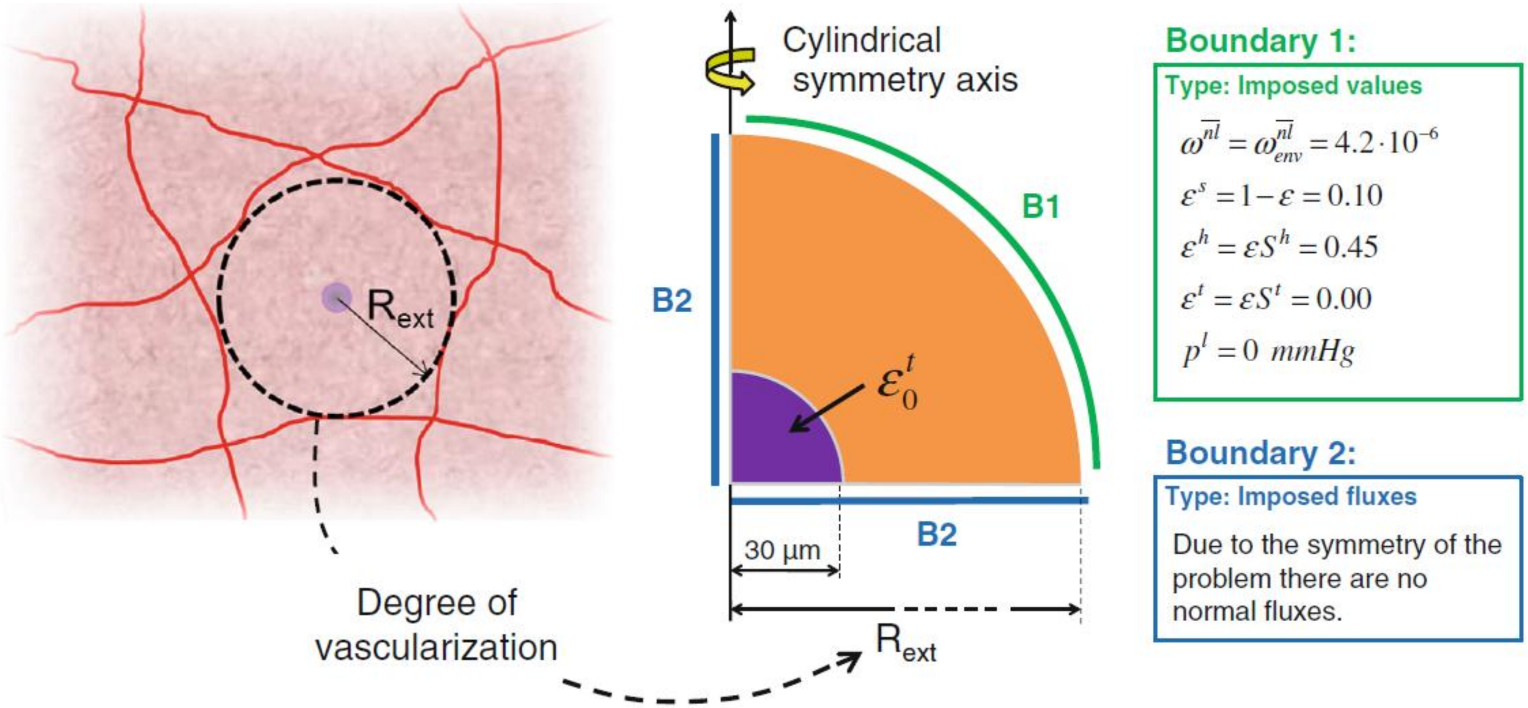


Numerical prediction of the volume fraction of the tumor cells (total and living volume fractions) during 360h (a); mass fraction of oxygen (b).



Optical Imaging of Prostate Tumor in Rat Model: the Fluorescent near-infrared probe (PSS-794) targets the necrotic core of the tumor

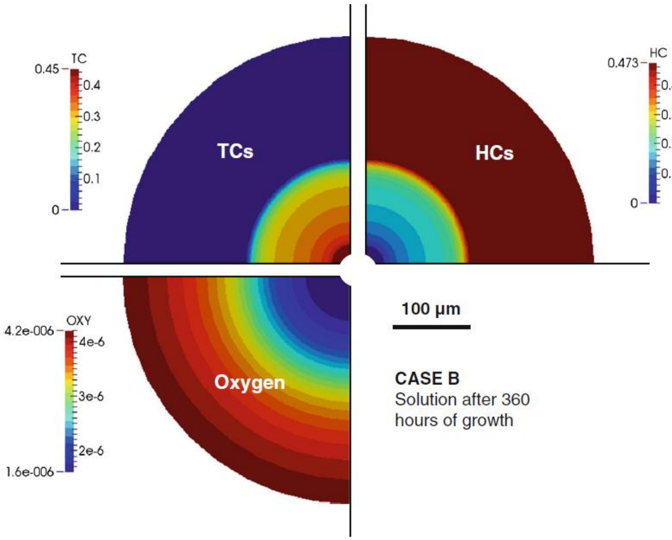
CASE 2: MTS *IN VIVO*

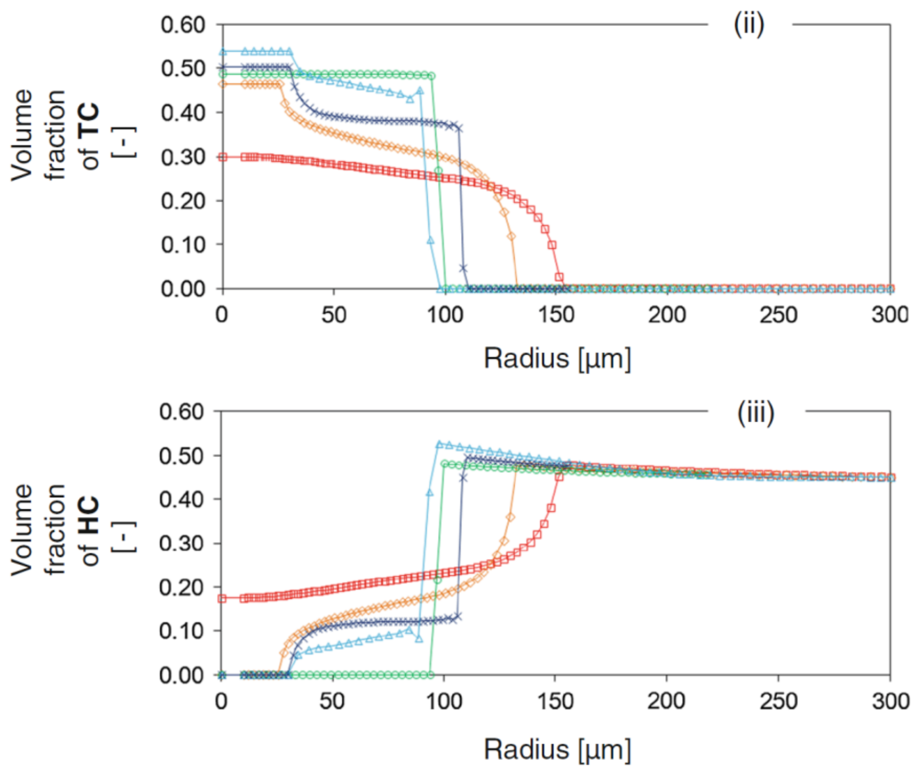


	σ_{hl} [mN/m]	σ_{tl} (mN/m)	σ_{th} (mN/m)	a_h (N/m^3)	a_t (N/m^3)	μ^h (Pa s)	μ^t (Pa s)
Case A	72.0	108.0	36.0	0.0	0.0	3.6×10^1	3.6×10^1
Case B	72.0	84.0	12.0	0.0	0.0	3.6×10^1	3.6×10^1
Case C	72.0	72.0	0.0	0.0	0.0	3.6×10^1	3.6×10^1
Case D	72.0	72.0	0.0	1.5×10^6	1.0×10^6	3.6×10^1	3.6×10^1
Case E	72.0	72.0	0.0	0.0	0.0	7.2×10^1	3.6×10^1

CASE 2: MTS *IN VIVO*

TC-HC interfacial tension has a relevant impact on growth and invasion!



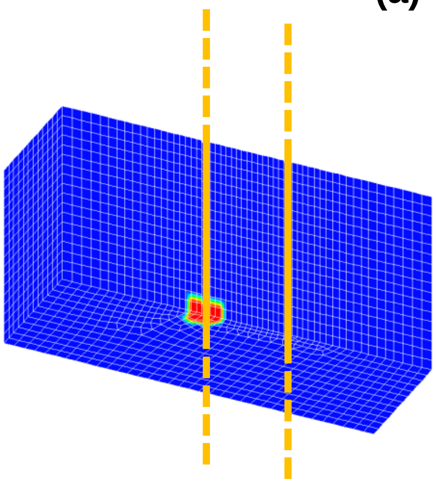


	σ_{hl} [mN/m]	σ_{tl} (mN/m)	σ_{th} (mN/m)	a_h (N/m^3)	a_t (N/m^3)	μ^h (Pa s)	μ^t (Pa s)
Case A	72.0	108.0	36.0	0.0	0.0	3.6×10^1	3.6×10^1
Case B	72.0	84.0	12.0	0.0	0.0	3.6×10^1	3.6×10^1
Case C	72.0	72.0	0.0	0.0	0.0	3.6×10^1	3.6×10^1
Case D	72.0	72.0	0.0	1.5×10^6	1.0×10^6	3.6×10^1	3.6×10^1
Case E	72.0	72.0	0.0	0.0	0.0	7.2×10^1	3.6×10^1

CASE 3: TUMOR CORDS

Two blood vessels are considered with the tumor present initially only in one vessel. In a first numerical simulation **(S1) the distance between the two vessels is 80 µm**, in a second one **(S2) the distance is 100 µm**

(a)



Blu zone:

$\omega^{\overline{nl}} = \omega^{\overline{nl}}_{env} = 4.2 \cdot 10^{-6}$

$\varepsilon^s = 1 - \varepsilon = 0.10$ $\quad \varepsilon^t = \varepsilon S^t = 0.00$

$\varepsilon^h = \varepsilon S^h = 0.40$ $\quad p^l = 0 \ mmHg$

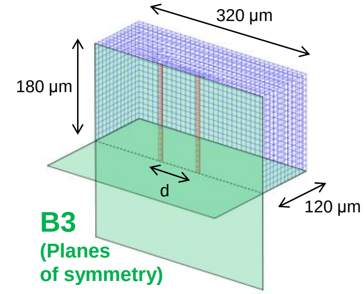
Red zone:

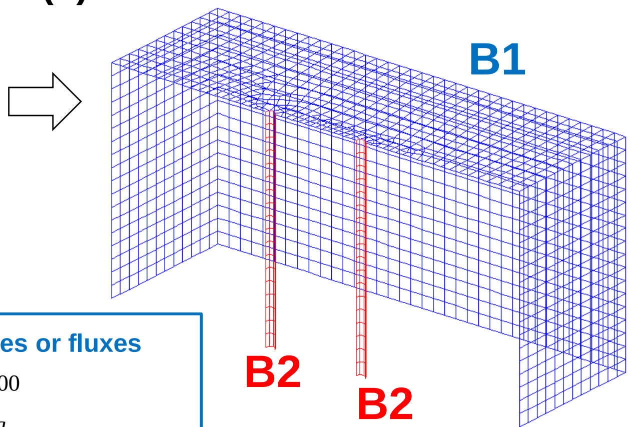
$\omega^{\overline{nl}} = \omega^{\overline{nl}}_{env} = 4.2 \cdot 10^{-6}$

$\varepsilon^s = 1 - \varepsilon = 0.10$ $\quad \varepsilon^t = \varepsilon S^t = 0.40$

$\varepsilon^h = \varepsilon S^h = 0.00$ $\quad p^l = 0 \ mmHg$

(b)





Boundary 1: Imposed values or fluxes

$\varepsilon^s = 1 - \varepsilon = 0.10$ $\quad \varepsilon^t = \varepsilon S^t = 0.00$

$\varepsilon^h = \varepsilon S^h = 0.40$ $\quad p^l = 0 \ mmHg$

Normal flux of oxygen equal to 0

Boundary 2: Imposed values or fluxes

$\omega^{\overline{nl}} = \omega^{\overline{nl}}_{env} = 4.2 \cdot 10^{-6}$

Normal flux of *t*, *h*, and *l* equal to 0

Boundary 3: Imposed fluxes

Due to the symmetry of the problem there are no normal fluxes.

(a) Initial conditions of the third case. Yellow shows the axes of the two capillary vessel

(b) Geometry and boundary conditions.

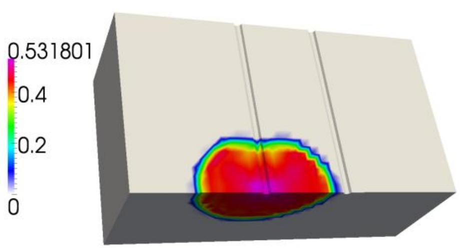
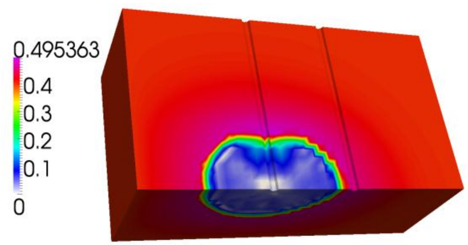
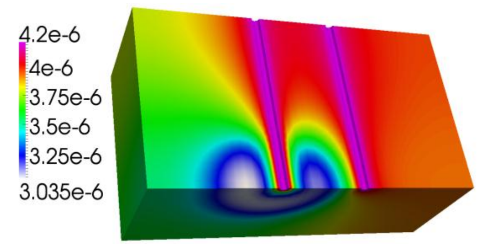
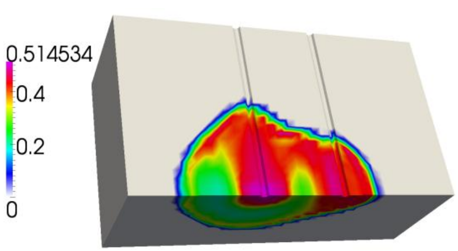
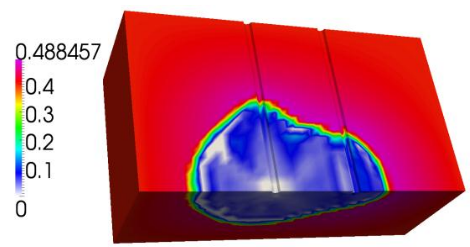
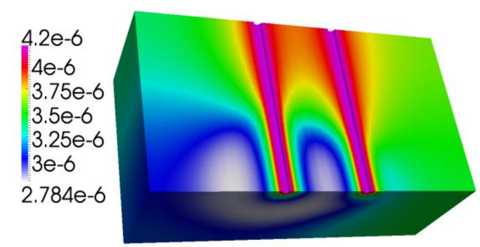
CASE 3: TUMOR CORDS

Two blood vessels are considered with the tumor present initially only in one vessel. In a first numerical simulation **(S1) the distance between the two vessels is 80 µm**, in a second one **(S2) the distance is 100 µm**

Case 3-S1: Tumor growth from 0 to 20 days

CASE 3: TUMOR CORDS

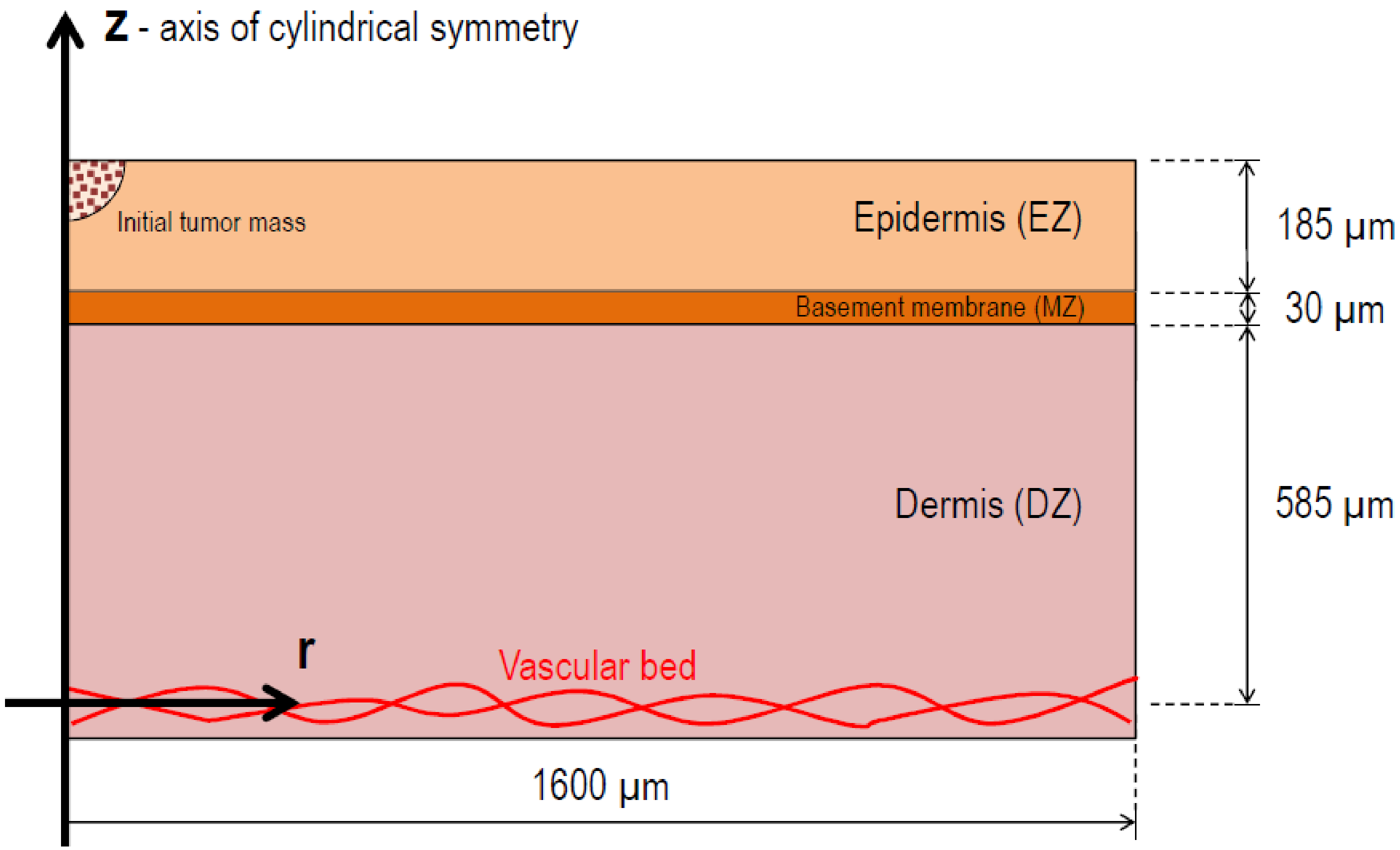
Two blood vessels are considered with the tumor present initially only in one vessel. In a first numerical simulation **(S1) the distance between the two vessels is 80 μm**, in a second one **(S2) the distance is 100 μm**

	Living tumor cells (LTC)	Host cells (HC)	Oxygen mass fraction
168 hours			
360 hours			

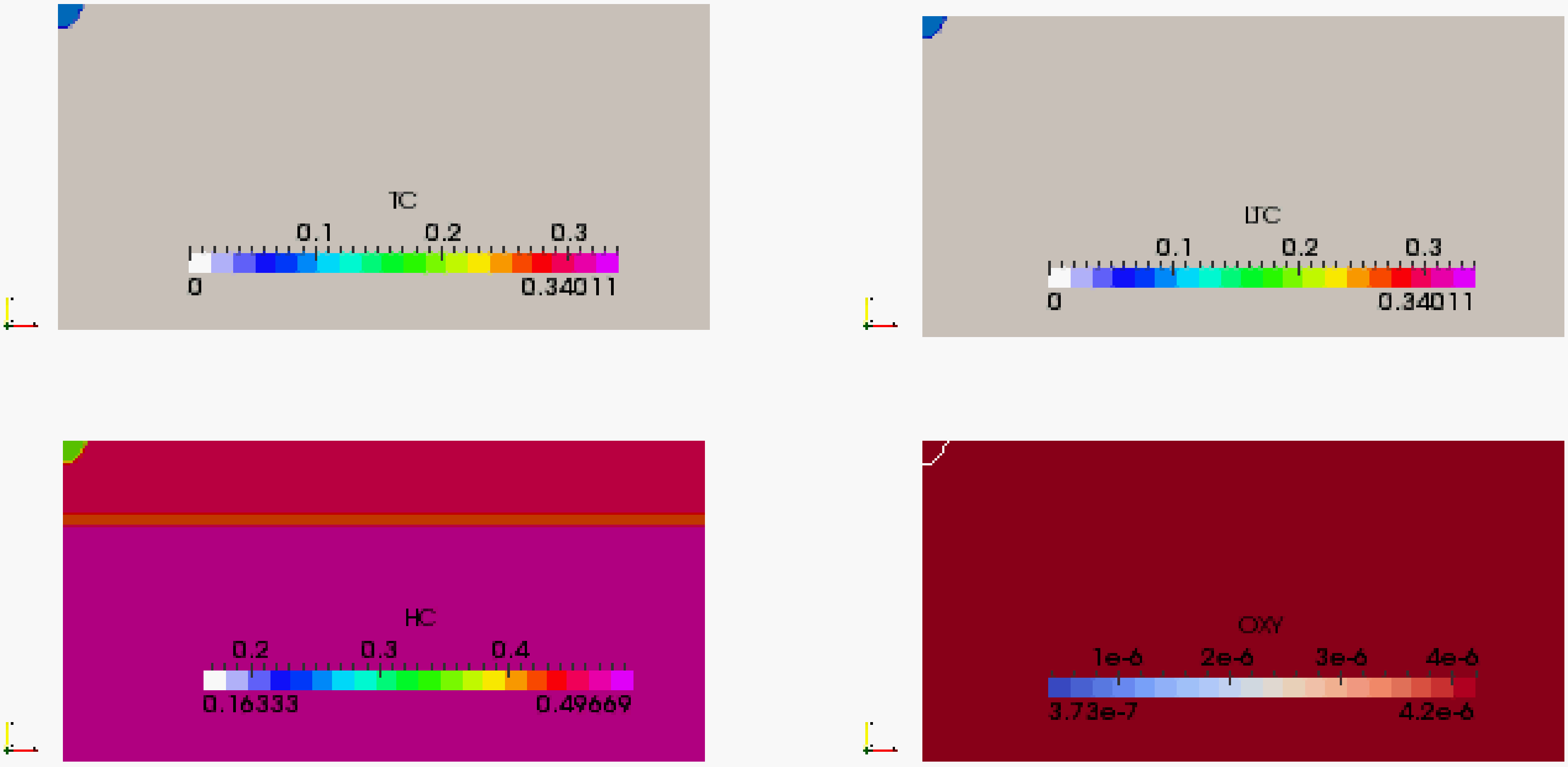
Volume fractions of the living tumor cells (first column) of the healthy cells (second column) and mass fraction of oxygen (third column) for the case S1.

CASE 4: GROWTH OF MELANOMA

Recently the assumption of a rigid scaffold has been relaxed and the impact of **ECM deformability** can be now properly **taken into account**

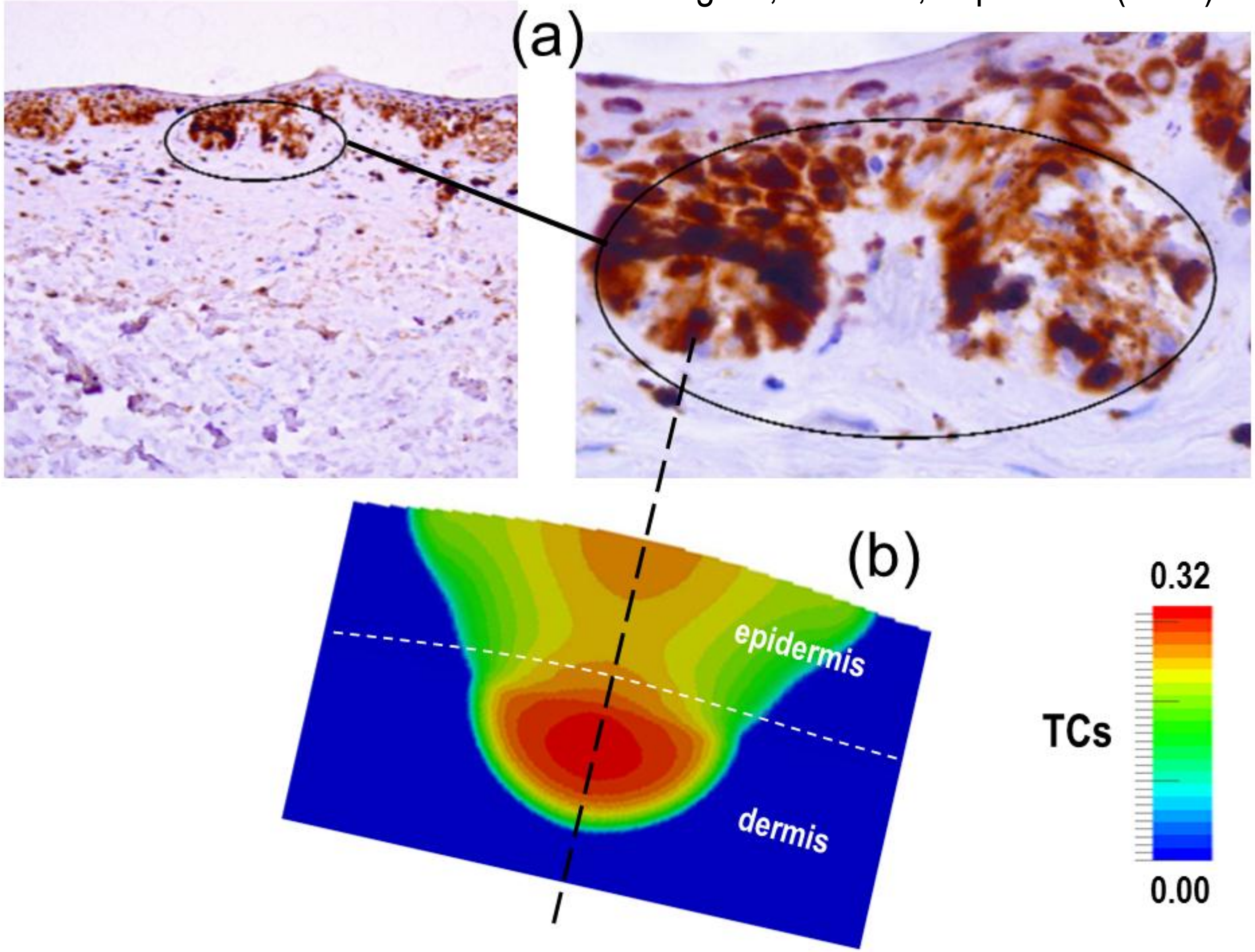


CASE 4: GROWTH OF MELANOMA



CASE 4: GROWTH OF MELANOMA

Chung LS, Man YG, Lupton GP (2010)



Concrete at early age

Tumor growth

General conclusions

THCM model young concrete

Conclusions

- The model, even if sophisticated, is reasonably exploitable for real life cases.
- Going from the material scale to the structural one an agreement between the numerical and experimental results is achieved qualitatively and quantitatively.

Perspectives

- The creep rheological model must be enhanced to take into account concrete age (long-term creep).
- Numerical results of the hydration dependent damage model must be confirmed by experiments, which are currently under design.

Tumor growth model

Conclusions

- A multiphase model for tumor growth in the avascular stage has been developed.
- Diffuse interfaces are considered with pressure differences between the three fluids;
- The computational procedure has a modular structure which allows to add new building blocks if needed (c_i, vasculature, T, pH…);

Perspectives

- Modeling of angiogenesis and introduction of vasculature, drugs delivery.
- Extensive validation with experiments.

Thank you for your attention!