GEMM
Group of Structural Mechanics and Materials Modelling

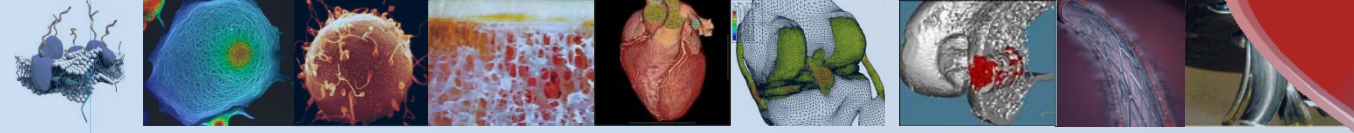
Mathematical modelling of wound healing processes to help the treatment of chronic wounds

Etelvina Javierre

In collaboration with:

Fred Vermolen, Sergey Zemskov (TU Delft)

Pedro Moreo, José Manuel García-Aznar (UZ)

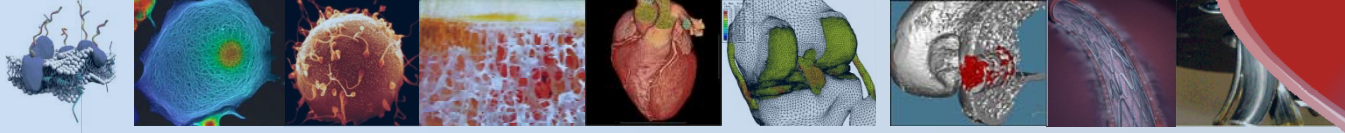


MEDICAL MOTIVATION

Open wounds compromise organ integrity by:

- decreasing the mechanical strength of surrounding tissue
- putting the immunology system at risk
- impairing organ function

Cancer as a wound that does not heal



MEDICAL MOTIVATION

Type of pathology	Number of patients per year		Total cost per year
Trauma	35.2 million	[USA data]	
Thermal injury	1 million	[USA data]	
Venous ulcers	600000	[USA data]	$ 5.8 Billion
Pressure ulcers	1.4 million	[USA data]	$ 2.2 Billion
Diabetic leg ulceration	670000	[EU data]	600 Million€
Prevalence of diabetic ulcers	6-7 million	[EU data]	> 5000 Million€
LEA in diabetic patients	65800	[EU data]	2.6 Billion€

References: Clark et al., J. Investigative Dermatology, 2007, vol. 127, pp. 1018-1029

Rasanen et al., Acta Orthop. 2007, vol. 78, pp. 108-115

INDUSTRIAL RELEVANCE

podoactiva®
CENTROS DE PODOLOGÍA Y BIOMECÁNICA

Podiatry services for profesional athletes, but also general clinical practice

Multidisciplinary team of podiatrists, physiotherapist, physicians and engineers

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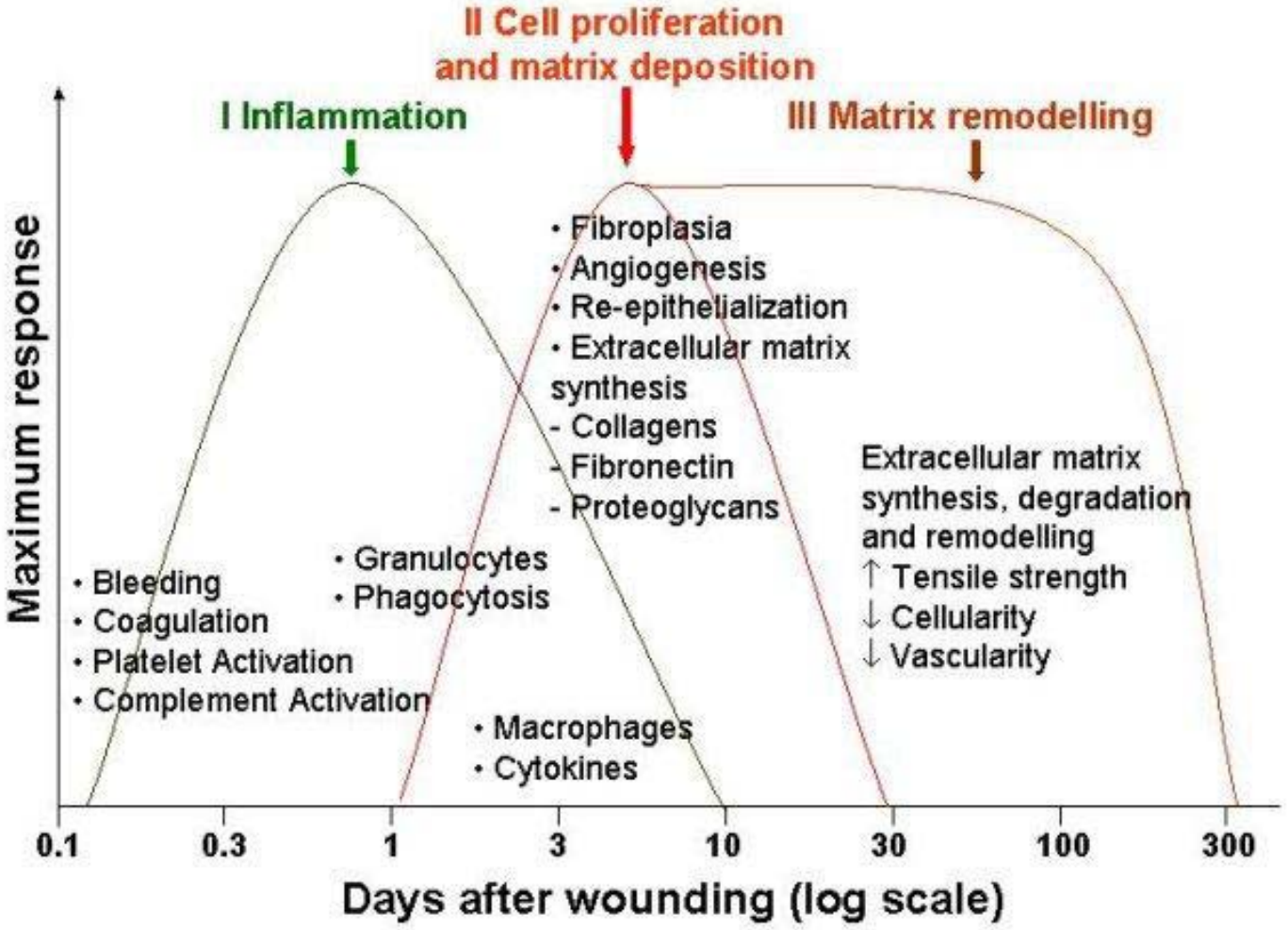
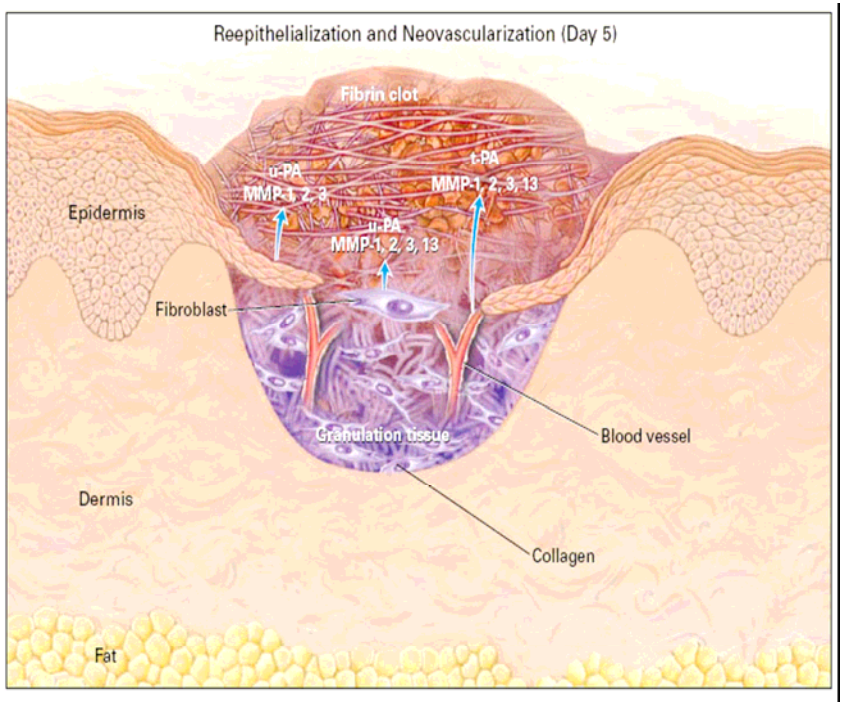
Patient specific prevention, prognosis and treatment of chronic pressure ulcers in diabetic patients through multiphysic and multiscale modelling

SEVENTH FRAMEWORK PROGRAMME

NORMAL WOUND HEALING



EVENTS THAT WE ARE GOING TO TARGET



1. Re-epithelialization
   - repair of the connectivity of the basal membrane
   - cell migration and mitosis triggered by released factors
2. Angiogenesis
   - repair of the vascular network
   - growth of vascular tips towards regions of low oxygen tension
3. ECM synthesis and wound contraction
   - cellular synthesis of ECM components
   - cell deformation and remodelling of ECM

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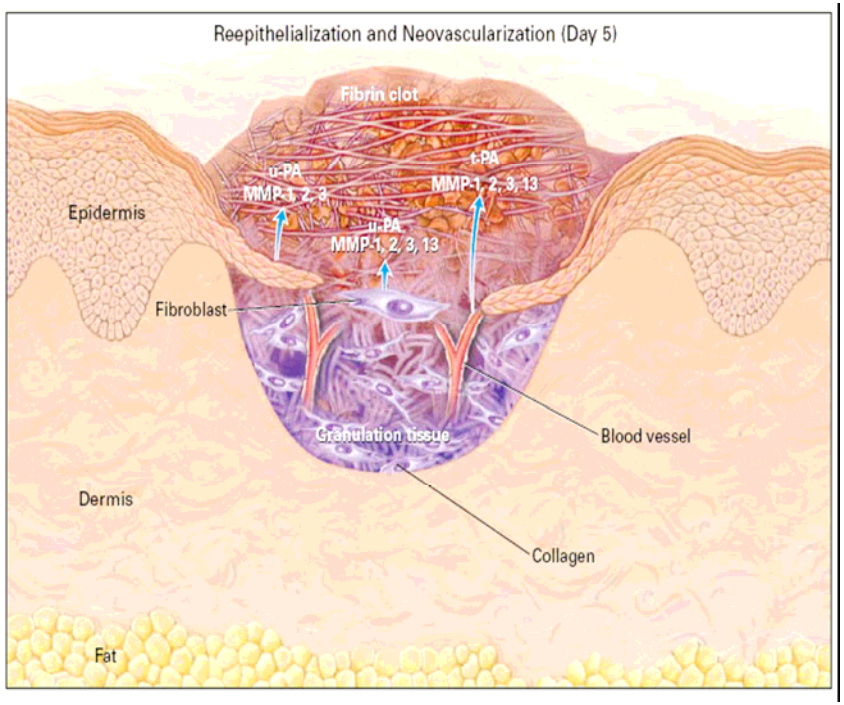

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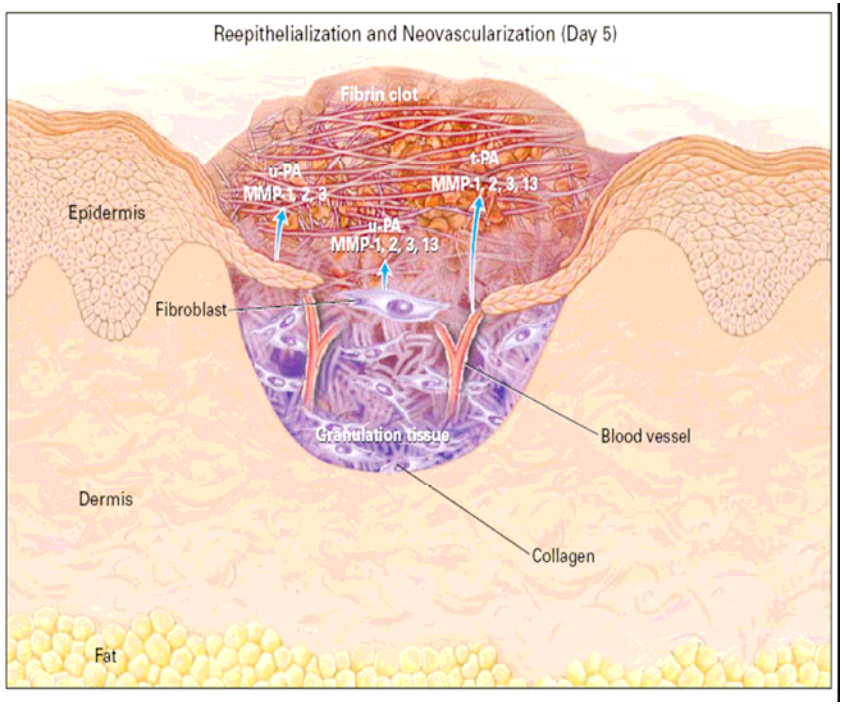

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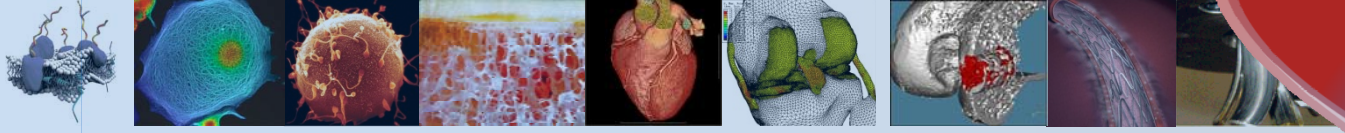
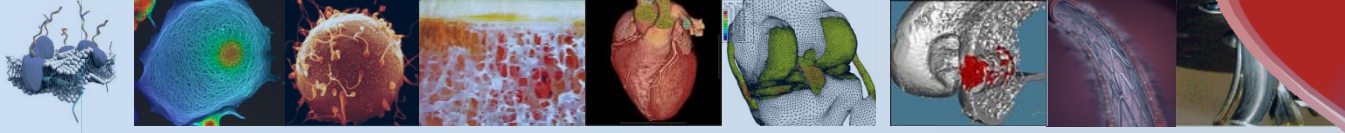


HOW ARE WE GOING TO MODEL THEM?

Coupled systems of convection-diffusion-reactions

Cellular species ⟷ Chemical biofactors ⟷ Extracellular matrix



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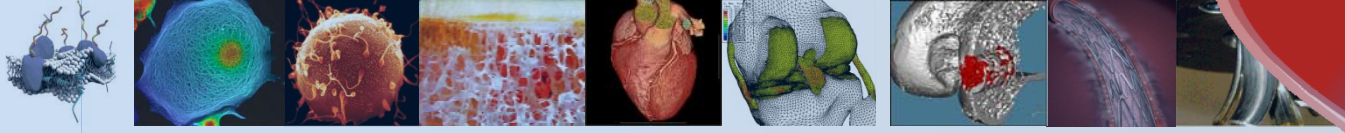
$$\frac{\partial n_i}{\partial t} = \nabla \cdot \left(D_i \nabla n_i - C_{ij} n_i \nabla c_j - n_i \frac{\partial \mathbf{u}}{\partial t} \right) + r(c_j, \theta) n_i \left(1 - \frac{n_i}{n_i^0} \right) + k_+ n_j - k_- n_k - \lambda_i n_i$$



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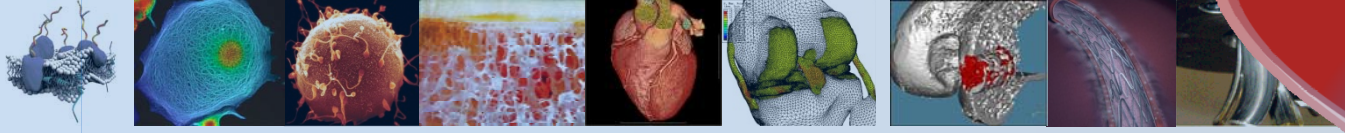
random dispersal



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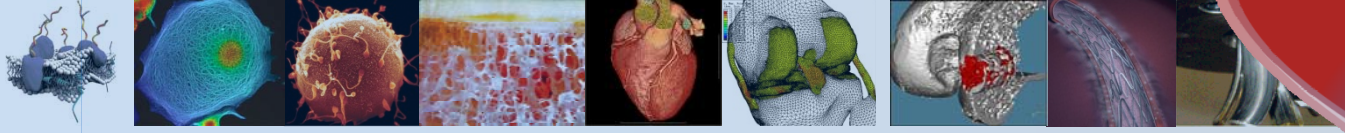
chemotaxis



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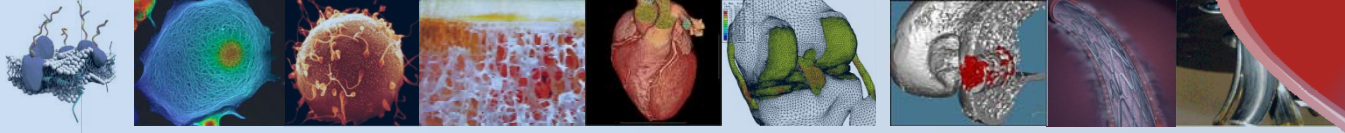
passive convection



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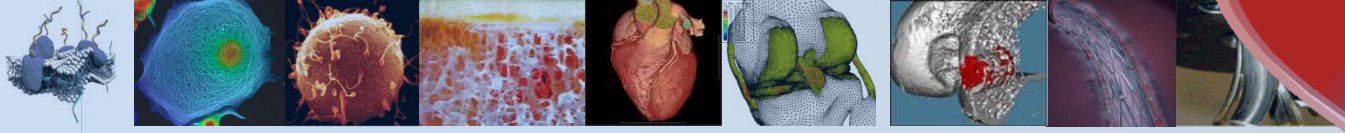
chemical and mechanical enhancement of proliferation



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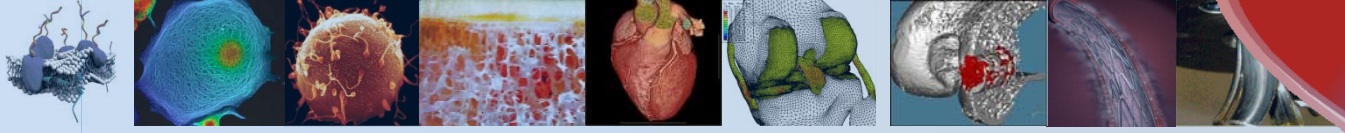
differentiation from other species



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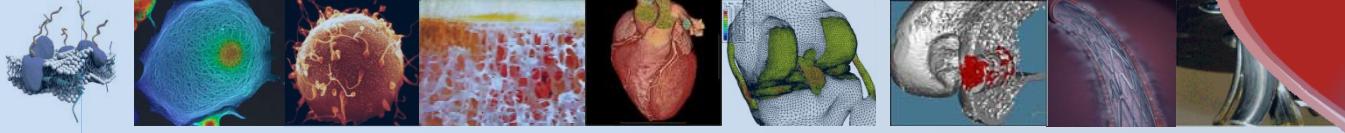
differentiation to other species



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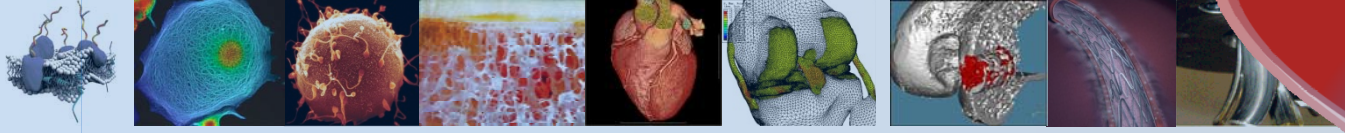
cell death



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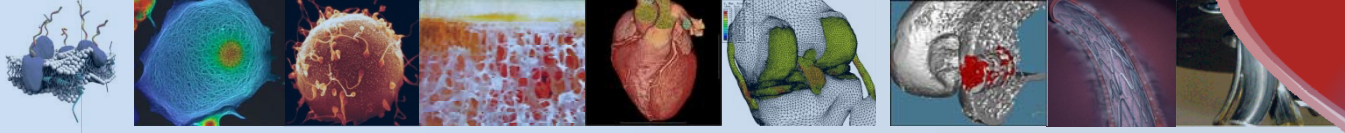

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rate of change of chemical species = chemical transport + chemical production - chemical depletion

$$\frac{\partial c_i}{\partial t} = \nabla \cdot \left(D_i^c \nabla c_i - c_i \frac{\partial \mathbf{u}}{\partial t} \right) + k_i^c (n_i + \xi n_j) \frac{c_i}{\Gamma_i + c_i} - \delta_{ij} n_j c_i - \lambda_i^c c_i$$

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diffusion

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cell production of chemical species

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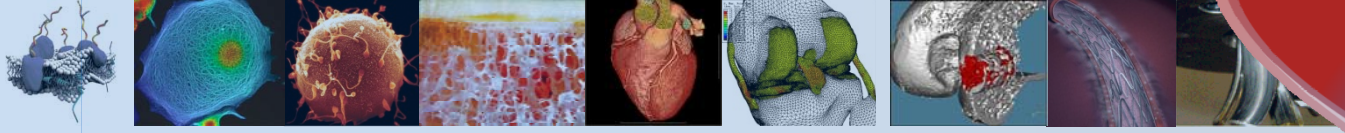
chemical uptake by cells



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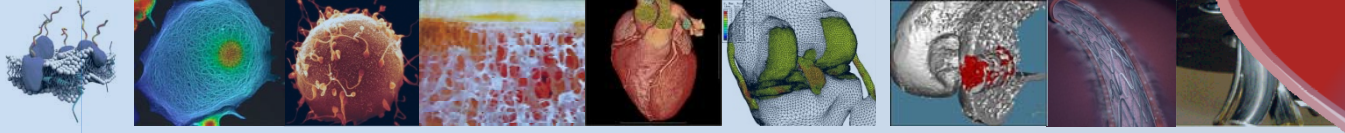
chemical decay



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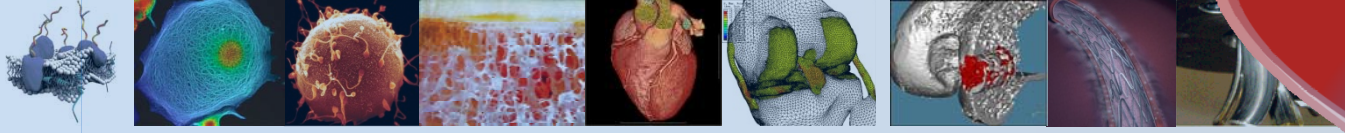
rate of change of ECM density = movement due to deformation + synthesis - degradation

body forces = ECM resistive forces + cell traction forces

$$s\rho\mathbf{u} = \nabla\cdot\left(\mu_1\frac{\partial\boldsymbol{\varepsilon}}{\partial t}+\mu_2\frac{\partial\theta}{\partial t}\mathbf{I}+\frac{E}{1+\nu}\left(\boldsymbol{\varepsilon}+\frac{\nu}{1-2\nu}\theta\mathbf{I}\right)+p_{cell}(\theta)\frac{n_i}{R_i^2+n_i^2}\rho\mathbf{I}\right)$$



NUMERICAL SOLUTION

- Self developed FE code in Matlab®
  - mesh generation
  - spatial discretization:
    - element matrices construction and assembly
  - temporal discretization: IMEM methods
  - moving boundaries
- Analysis to be conducted
  - healing of planar and circular wounds in 1D
  - sensitivity analyses to identify crucial parameters
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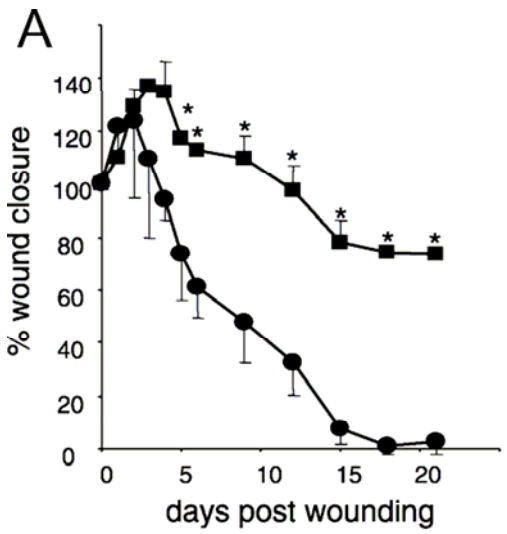
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