Models of emergent networks

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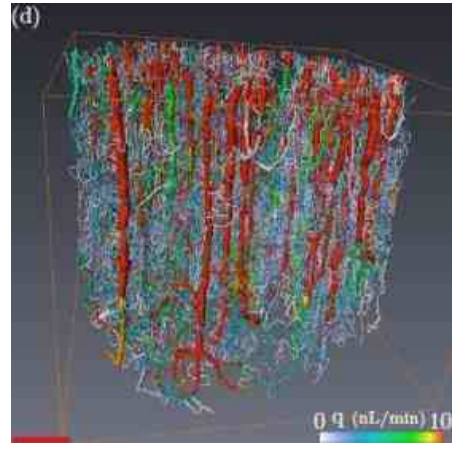
Summary

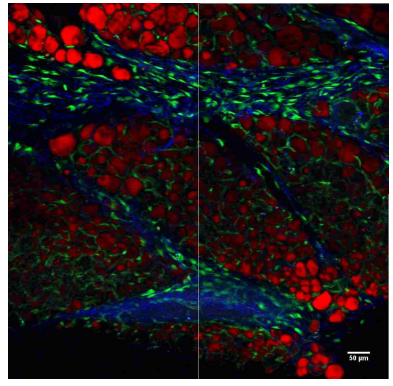
1. Introduction

Complex network features

Large size



Fuzzyness



Plasticity

Goal: model evolving networks

ex: ant trails, sheep trails, ...

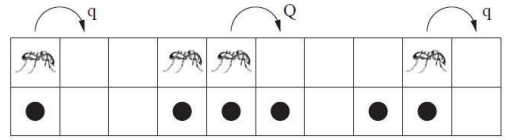
2. Ant trail networks

with E. Boissard, S. Motsch (ASU)

Boissard, D., Motsch, J. Math. Biol., 66 (2013), pp. 1267-1301.

Ant-trail models: literature

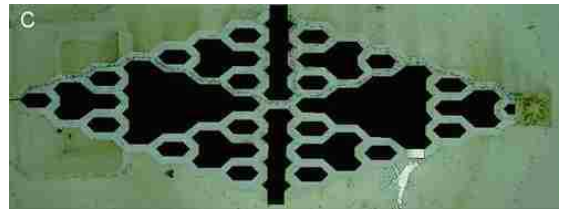
Motion on a pre-existing trail



Cellular automata

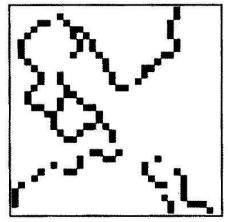
[John et al, JTB 04; Nishinari etal, Physica A 06]

Decision-making between trails



ODE's [Reid et al, J. Exp. Biol 11]

Zero-dimensional models



Trail density [Edelstein-Keshet, JMB 94]

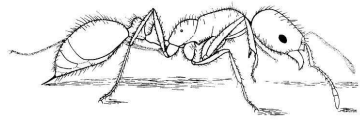
Lattice or cellular automata models

[Watmough & EK, JTB 95; Rauch et al Phys. Lett. A 95;

Schweitzer et al, Biosystems 97; Vincent etal JMB 04]

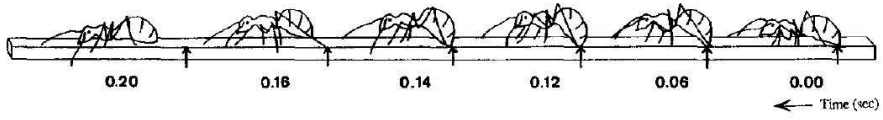
Trail-laying

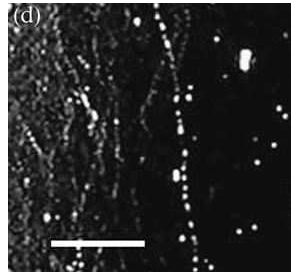
Ants lay pheromones with sting



continuous or discrete streaks

Diffusion

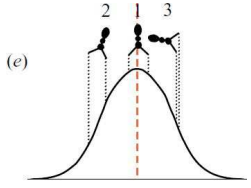


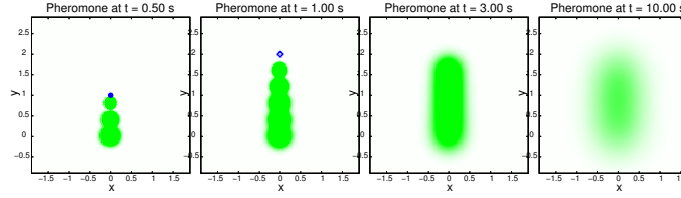


connects neighboring streaks

Pheromone density $\rightarrow$ mountain ridge

pheromone density gradient sensing

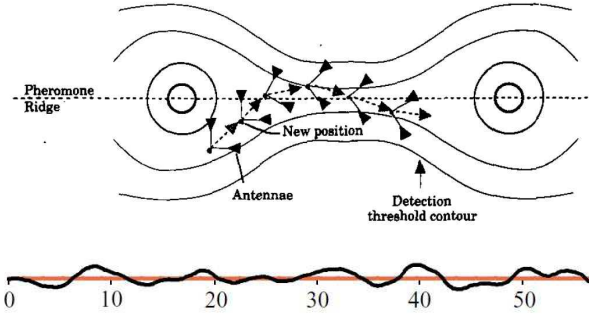




with antennas

orients towards pheromone gradient

undulatory motion about ridge crest



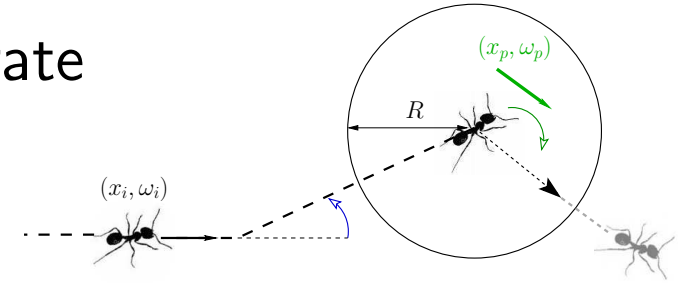
Main model assumptions

Pheromones are directed quantities

Segment connecting two consecutive phero deposits

Two-particle species: ants and trails

- ants move at constant speed
- ants subject to random direction changes
- ants interact with neigboring trails through alignment
- ants deposit trails at a constant rate
- trails evaporate at a constant rate



Goal:

Individual-Based model $\rightarrow$ observe emergence of trails

kinetic and hydrodynamic models

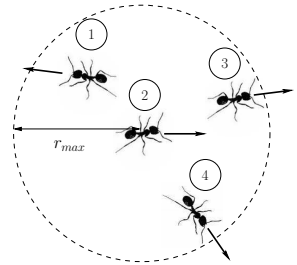
Trail statistics

Trails defined by clustering relation

$$P_i \sim P_j \iff |X_i - X_j| \leq r \quad \text{and} \quad |\sin(\widehat{\omega_i, \omega_j})| \leq s$$

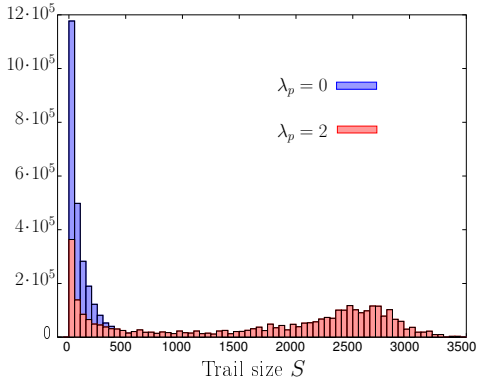
r and s ad-hoc parameters; P_i refers to ants or trail elements closed into equivalence relation by transitivity

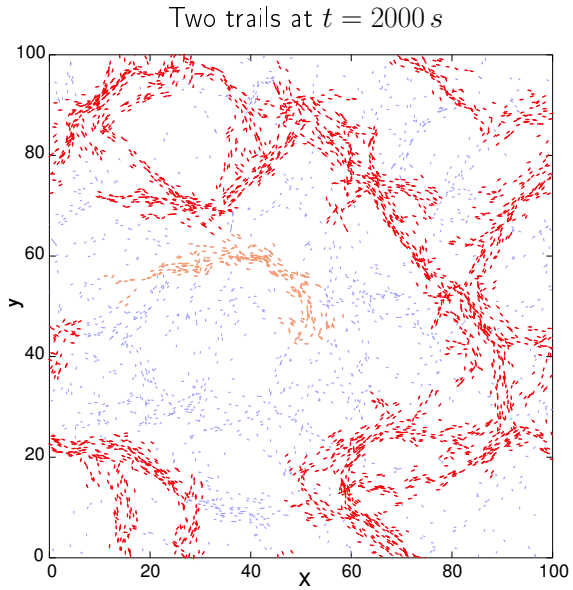
trail = equivalence class of this relation



Trails size statistics

$p_t(S) =$ proba that a particle P_i belongs to a cluster of size S



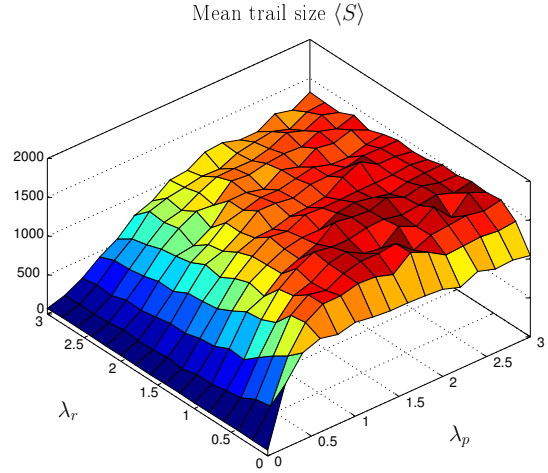


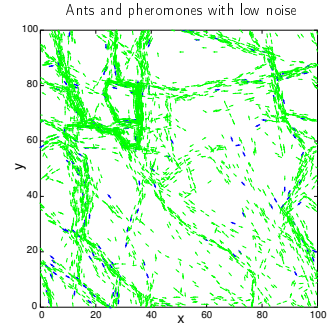
Emergence of trails: phase transition

Mean trail size $\langle S \rangle = \sum_S S\, p_t(S)$

Abrupt increase when trail recruitment freq. increases

phase transition





Trail width

From lateral decay of two-point correlation f_2

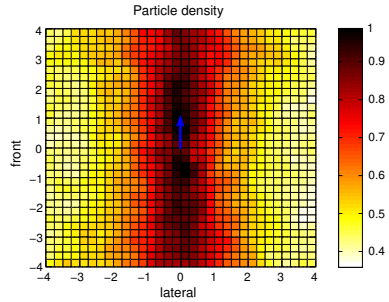
trails are thinner with

more trail recruitment

less random jumps

λ_p	r_0 (cm)
3	2.796
2	3.181
1	4.350

λ_r	r_0 (cm)
0	2.532
1	2.964
2	3.181
3	3.345



3. Blood capillary network

with P. Aceves-Sanchez, B. Aymard (Nice), D. Peurichard (INRIA Paris),
L. Casteilla & A. Lorsignol (Stromalab, Toulouse),
P. Kennel & F. Plouraboué (Fluid Mech. Toulouse)

in preparation

Goal:

Explore possible mechanisms of vascular and capilary networks self-organization in tissues

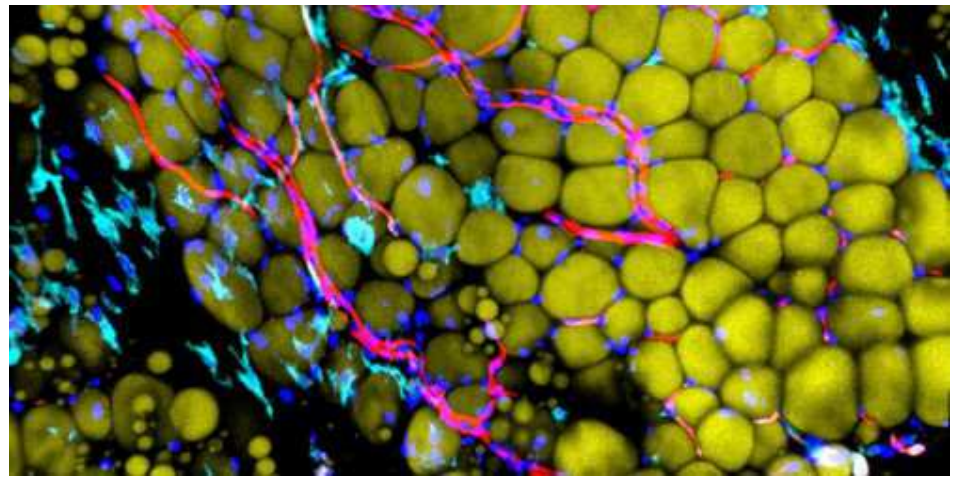
Motivations:

Tissue regeneration

Tissue engineering

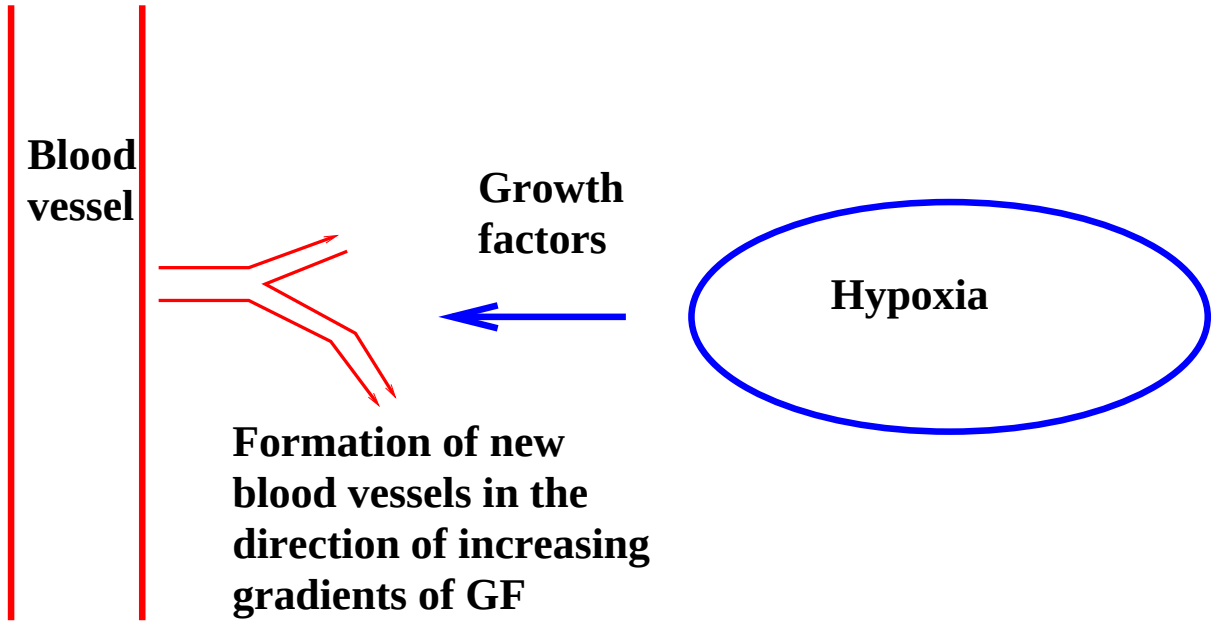
Tumors

Diseases

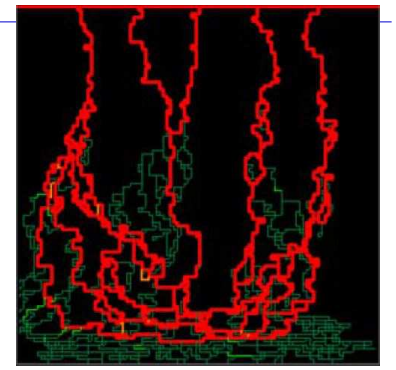


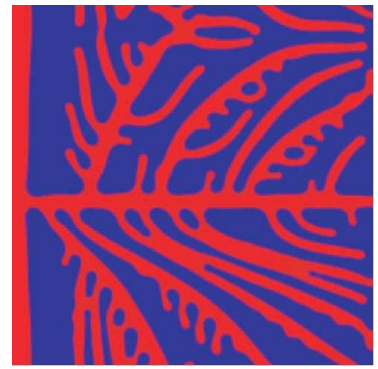
Related problem: tumor angiogenesis

Mechanism:



Models of vasculo/angio-genesis





Cell-based models

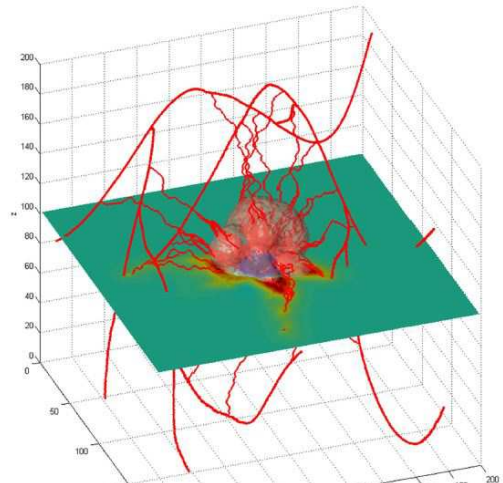
- Capilary = sequence of endothelial cells
- Model endothelial cell migration

Cell-based models with blood flow coupling

- Chaplain & coworkers, Maini & coworkers
- Travasso et al, PlosOne 2011
- Tang et al, Plos One 2014

Cell-based models with ECM (cellular Potts model)

- Bauer et al, PlosCB 2009
- Daub & Merks, Bull. Math. Biol. 2013



Models of vasculo/angio-genesis (II)

Network-based models

Schneider et al, Medical Image Analysis 2012

Secomb et al, PlosCB 2013

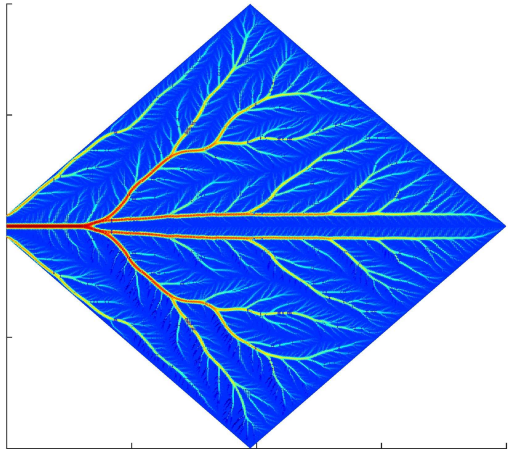
Macroscopic models

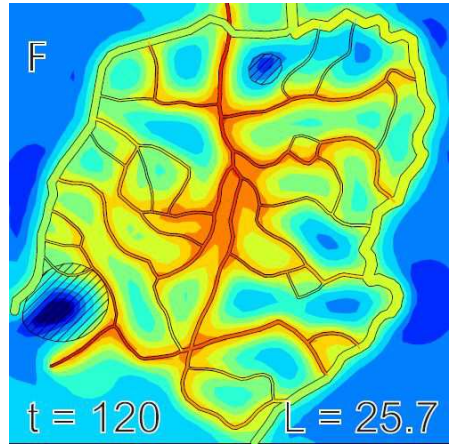
Orme & Chaplain, Math. Comput. Mod. 96

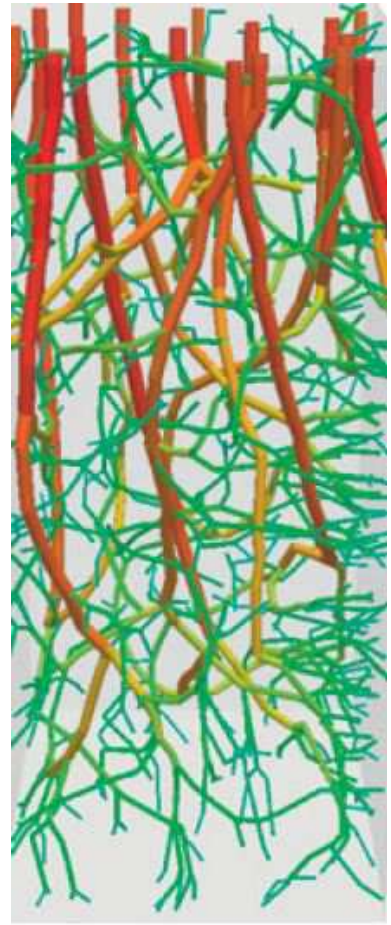
Billy et al, JTB 2009

Hu & Cai, PRL 2013

Haskovec et al, Nonlinear Anal 2016







Observations

Very detailed modelling of the background biology

- Pro: good quantitative agreement
- Con: difficult to disentangle influences of $\neq$ phenomena

Cell-based approaches suffer from directional bias

- unless very fine grid is used

Network-based approaches are complex to implement

- need to keep track of the connectivity

Our approach

Look for "minimal model"

- with as few agents and phenomena as possible
  - blood / interstitial fluid
  - oxygen (as a surrogate for any kind of nutrient)
  - capillaries
- No growth factor included

Capillaries $\equiv$ discrete directional entities

- $\sim$ network-based models
- $\not\sim$ without connectivity constraint
- "Fuzzy" connectivity by averaging

Inspired from ant-trail formation model

- [Boissard, D., Motsch, JMB 13]

Model features

Two-dimensional

- No obstruction to extend it to 3D

One discrete agent type: capillary segments

- Fixed length L

Two continuum fields

- Blood/interstitial fluid pressure $p(x,t)$
- Oxygen / nutrient concentration $\rho(x,t)$

Blood/interstitial fluid satisfies Darcy's law

$$u = -K\nabla p, \qquad \nabla \cdot u = 0$$

$u(x,t)$: fluid velocity
$K = K(x,t)$: hydraulic conductivity matrix
Bndry cond: Dirichlet, Neumann, periodic ...

Oxygen concentration: convection diffusion eq.

$$\partial_t \rho + \nabla \cdot (\rho u) - \nabla \cdot (D \frac{\rho}{\rho + \rho^*} \nabla \rho) = -\beta(\rho)\rho$$

Convection by fluid velocity u
Diffusion with diffusivity tensor $D(x,t)\frac{\rho}{\rho+\rho^*}$
Consumption by tissue at rate $\beta(\rho)$ (e.g. Menten-Michaelis)

Capillary dynamics

Capillary = discrete segment represented by

Position $X_i \in \mathbb{R}^2$, Direction $\omega_i \in \mathbb{S}^1$

Capillary creation: of capillary (X, ω): Poisson process

branching in direction of O_2-gradient $\omega = \nabla\rho/|\nabla\rho|(X)$

at X where O_2 concentration gradient $\nabla_x\rho(X)$ large

but O_2 concentration $\rho(X)$ not too large

reinforcement with flow direction $\omega = u/|u|(X)$

at X where flow $(\rho u)(X)$ neither too small nor too large

branching off in direction $\perp$ to flow $\omega = u^\perp/|u|(X)$

at X where maximal wall shear stress i.e. leading eigenvalue of $(\nabla_x u + (\nabla_x u)^T)(X)$ is large

Capillary destruction: increases with square of hydraulic conductivity $K(X) \Rightarrow$ large capillary density penalized

Capillary / blood - O_2 coupling

Capillary / Blood coupling

Through hydraulic conductivity matrix

$$K(x,t) = k_h \mathrm{Id} + \sum_{j \text{ s.t. } |X_j - x| \leq L} \kappa \; \omega_j \otimes \omega_j$$

Capillary / Oxygen coupling

Through diffusivity matrix

$$D(x,t) = \Delta_h \mathrm{Id} + \sum_{j \text{ s.t. } |X_j - x| \leq L} \Delta \; \omega_j \otimes \omega_j$$

Some remarks

Presence of a capilary segment at a point
- enhances hydraulic conductivity in its direction
- favors flow in its direction
- is reinforced by new capillary creation

Leads to larger vessels:
- Formed of several nearby parallel capilaries
- but size limited by capillary removal at high capillary density

Large blood flow in vessels:
- induces Oxygen gradients across vessels
- increases wall shear stress
- both trigger splitting / sprouting

The topology at junctions:
- becomes an emergent property, not hardwired in the model

Blood flow (Darcy's eq.)

Q^1-conforming finite element on square mesh

Oxygen concentration (convection-diffusion eq.)

Particle method

Diffusion velocity method [D. Mustieles, SISC 1990]

$$\rho(x,t) \approx \rho^N(x,t) = \sum_{i=1}^{N} m_i \delta\big(x - Y_i(t)\big),$$

m_i = Const

$$\dot{Y}_i(t) = \Big(u - D\frac{\nabla \rho_h^N}{\rho_h^N + \rho^*}\Big)(Y_i(t),t)$$

ρ_h^N is a smoothing of ρ^N using a kernel $W_h(x)$:

$$\rho_h^N(x,t) = \sum_{i=1}^{N} m_i W_h(x - Y_i(t))$$

Oxygen particles

- Introduced through artery wall with constant uniform weight
- Removed randomly according to consumption rate β
- Removed when reaching the vein wall

Capillary creation during time step Δt

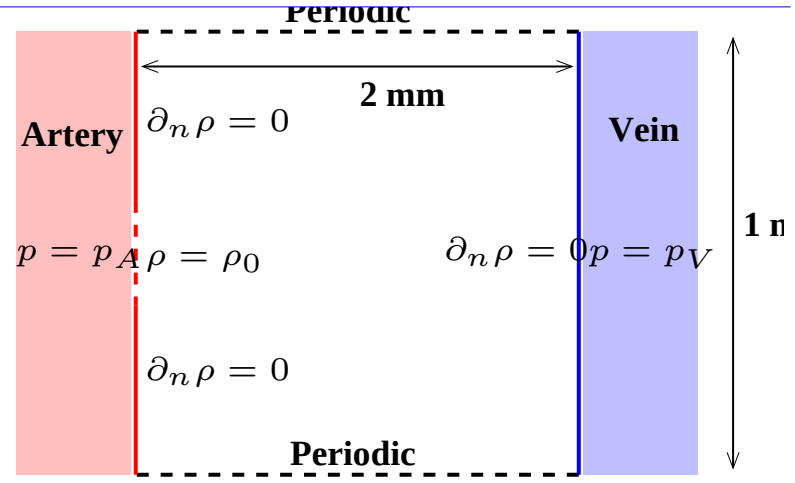
- Fix a maximal number N_c of new capillaries to create
- pick creation location X randomly with uniform proba
- Compute creation rate $\nu_c(X)$ at location X
- Create capillary at X with proba $1 - e^{-S\nu_c\Delta t}$
  - with $S = \text{Surface(Domain)}/N_c$

Capillary removal

- Remove randomly with proba $1 - e^{\nu_d\Delta t}$

Simulation conditions

Domain geometry



Parameters: measured

$p_A = 37.7$ mmHg; $p_V = 14.6$ mmHg

$\beta =$ Hill function with $\beta_{\text{sat}} = 0.01$ mn^{-1} μm^{-2}

$k_h = 400\,\mu\text{m}^2\text{mn}^{-1}\text{mmHg}^{-1}$; $\Delta_h = 10\,\mu\text{m}^2\text{mn}^{-1}$

Parameters: estimated

ρ_0 reference value; $\rho_s = \rho_0$; $\rho^* = \rho_0/10$

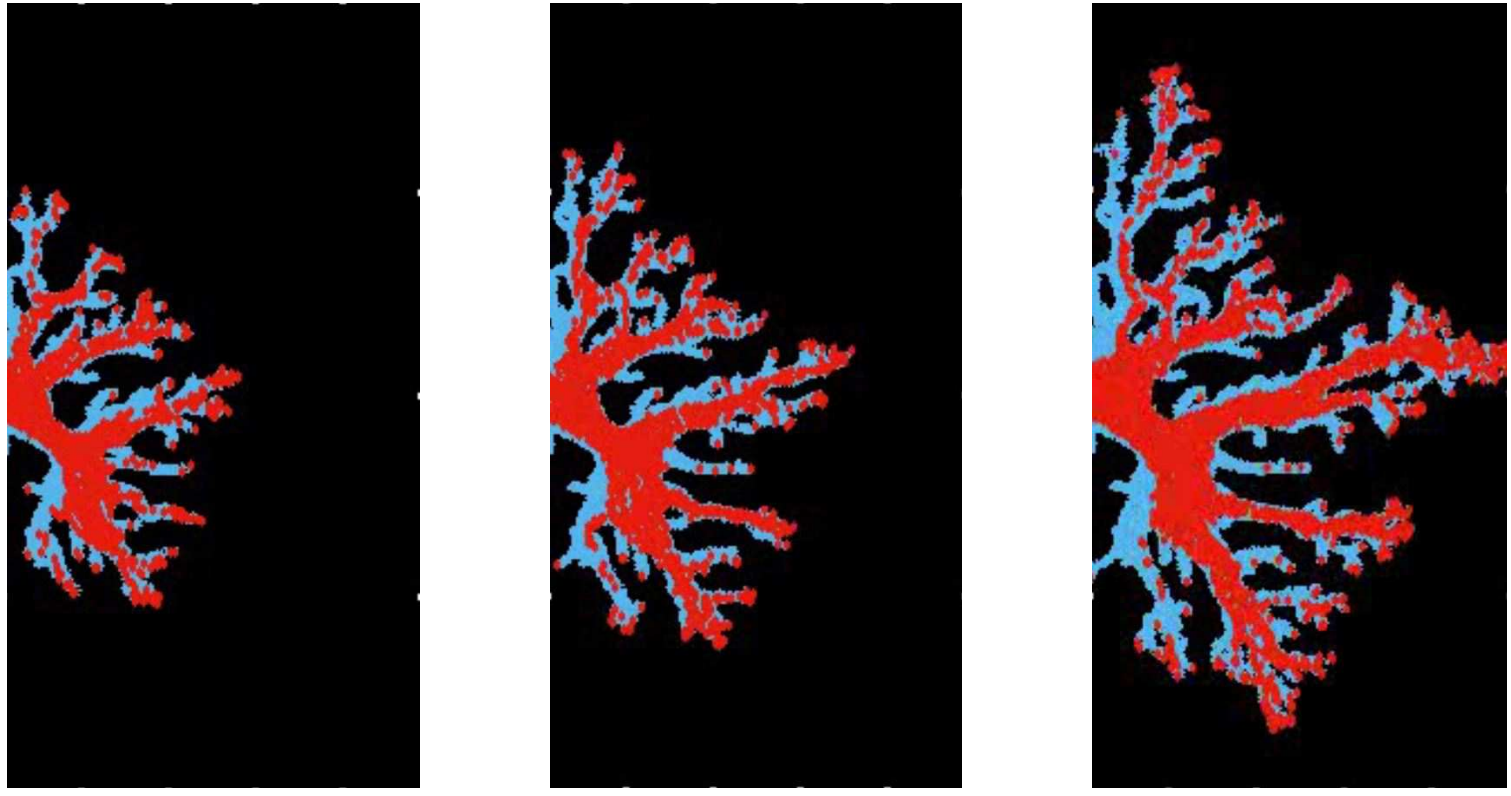
$\kappa = 200\,k_h$; $\Delta = 20\Delta_h$

capillary length $= 15\,\mu$m; width $= 4\,\mu$m; $N_c = 2\,10^5/\Delta t$

$\nu_c^* = 0.05\,\mu\text{m}^{-2}\text{mn}^{-1}$; $\nu_f^* = 0.01\,\mu\text{m}^{-2}\text{mn}^{-1}$

$\nu_d^* = 0.3$ mn^{-1}

Results

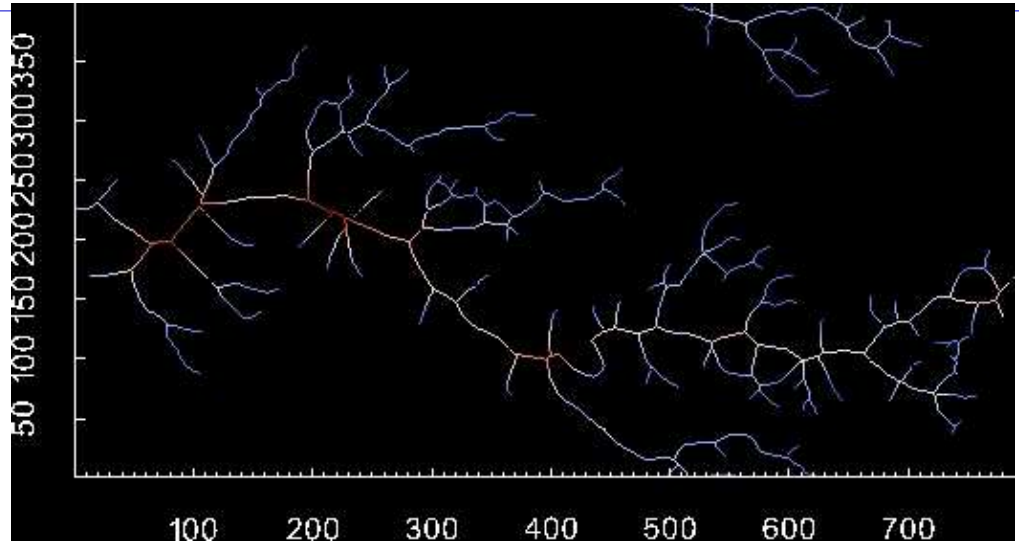


Salient features:

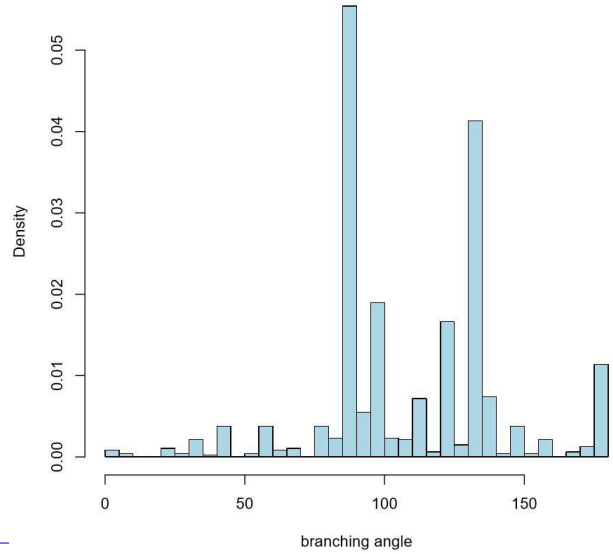
- Emergent vessel formation
- Sponteneous sprouting & branching

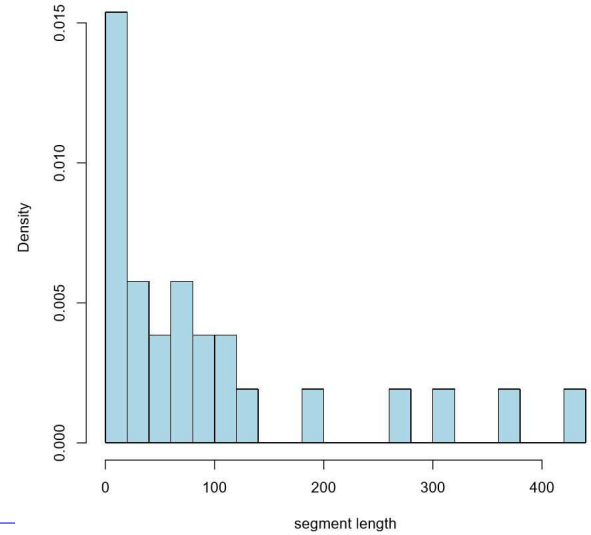
Statistics

Skeletonization



Branching angle / Segment length statistics





4. Fiber networks in tissues

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4. Conclusion

Conclusion

New "fuzzy network" technique

- Discrete items carry directional information
- Connectivity recovered by local averaging

Suitable for

- Dynamic topology
- Evolving networks
- Emergent networks

Simple modelling allows for

- Coarse-graining into macroscopic model
- Macro models for cross-linking fibers [M3AS 2015]