



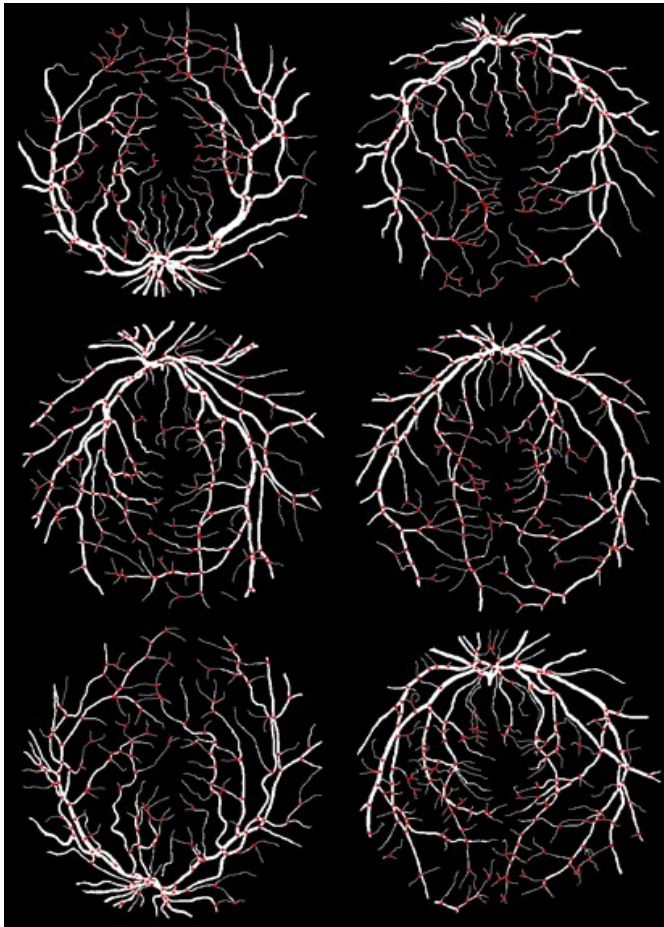
Hypoxia in vascular networks: a complex system approach to unraveling the Diabetes paradox

Yerali Gandica , Tobias Schwarz , Orlando Oliveira and Rui Travasso

Center for Computational Physics, Department of Physics, University of Coimbra, Portugal



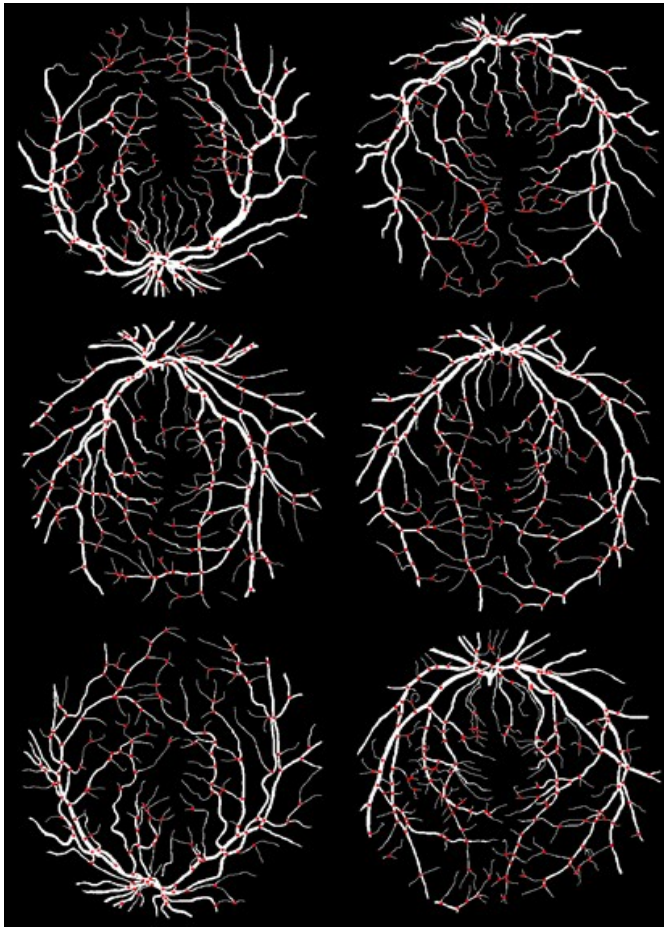
Vascular networks: Spatial networks



**Cost associated to the length
of vessels when delivering
energy, water or nutrients**

Blood flux is a conservative flux

Vascular networks: Spatial networks

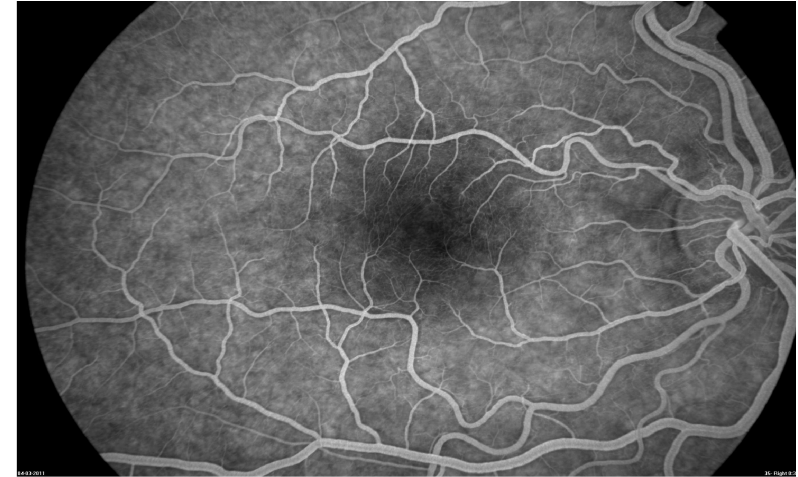


Two different topologies:
Major vessels: arterioles and
venules: blood transport.
→ fractal tree-like
Capillaries: nutrient and
oxygen diffusion:
→ \approx lattice structure.

We investigate tissue irrigation and hypoxia levels resultant from the damaged retinal vascular network due to Diabetic Rethinopathy.

Settings:

- Angiography of a human retina.
- Vessels \approx cylindrical symmetry.
- Blood viscosity high enough to neglect turbulence and non-linear effects.
- Steady state study
- The transport of oxygen: diffusive process.



DR: Two main stages with different phenotypes.

NPDR: inflammation in the capillaries and arterioles. Vessel malformations. Vessel blockage (No irrigation in some regions).

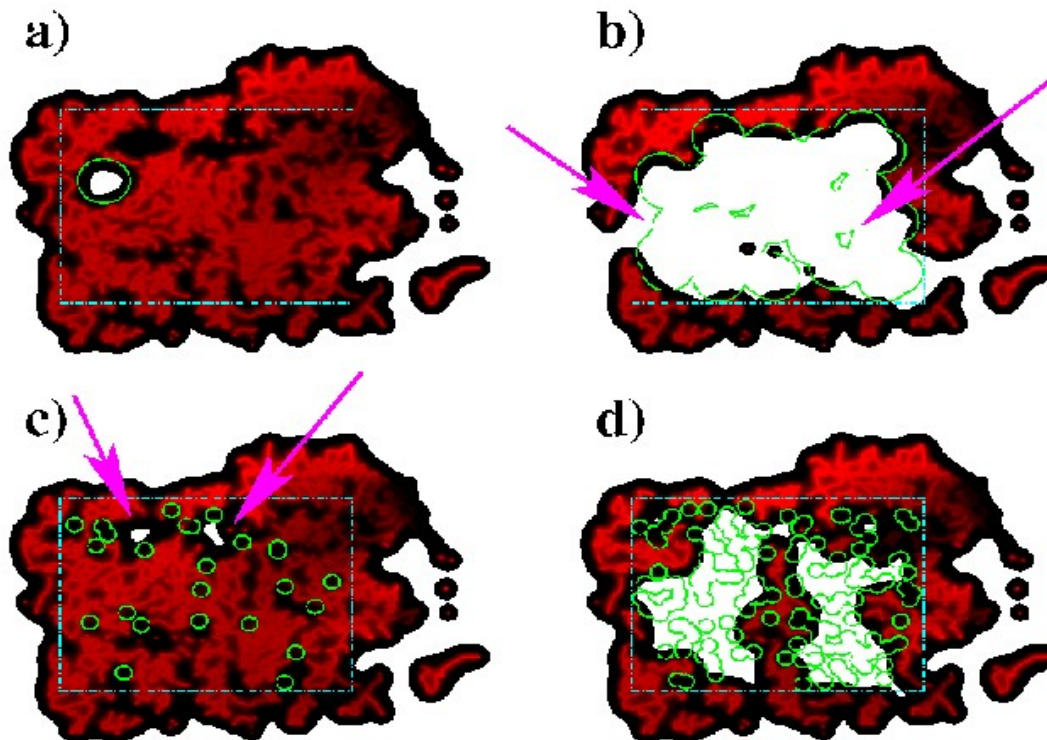
PDR: neovascularization, the growth of abnormal (fragile and leaky) new blood vessels.

Paradox: if the action in DR is the regression, disruption and blockage of blood vessels, then how does the hallmark of the most advanced stage of the disease is a very high vascular density?

Proteins Ang-2 hinder the function of the thinner vessels
(increase their permeability and render them non functional)

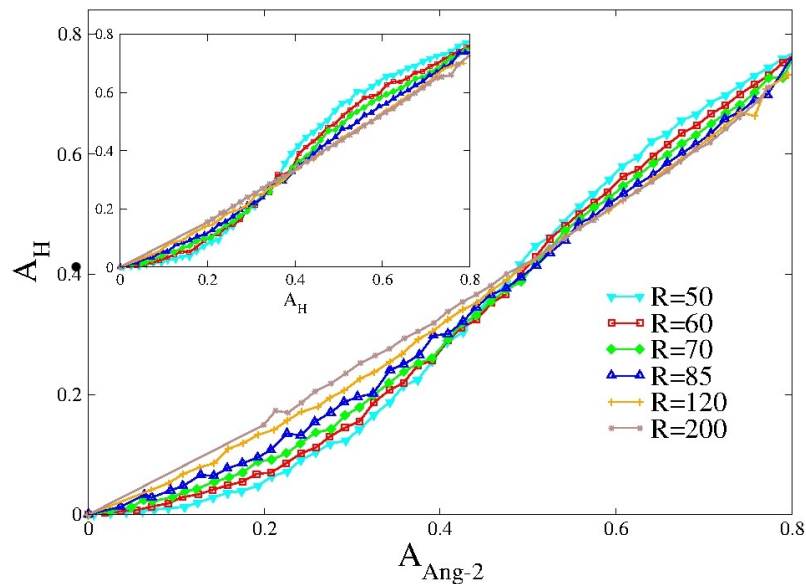
We consider randomly distributed small circular regions of radius R
→ where these proteins damage the vessels.

Inside these regions, we block all vessels with diameter smaller than a cutoff, Λ .

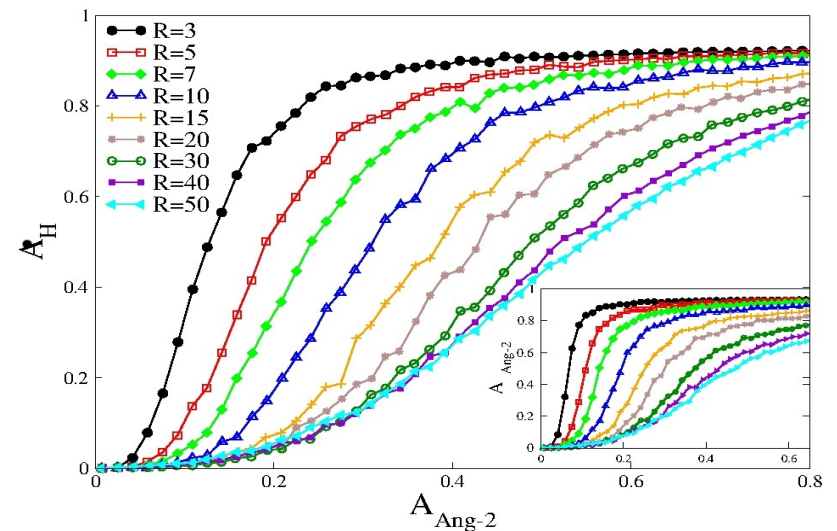


What we found

We found two regimens delimited by a critical Ang-2 spots radius.



Radius > 50 lattice units



Radius < 50 lattice units

Fraction of area in hypoxia (A_H) versus fraction of area in retina affected by Ang-2 Protein.

The critical Ang-2 spots radius, R_c ,



The characteristic irrigation length of the network.



Network spatial features



The largest distance that an irrigated point in the tissue is from its nearest vessel.

Blockage with Ang-2 spots of radius $>$ larger than R_c , the pro-angiogenic factors will only work in correcting the malformations provoked by the Ang-2 \rightarrow **non-proliferative diabetic retinopathy phenotype.**

Targets of radius $<$ R_c : may lead to hypoxia in regions with functional vessels \rightarrow the tissue will produce pro-angiogenic factors \rightarrow creation of neo-vessels in regions with functional vasculature \rightarrow **proliferative diabetic retinopathy phenotype.**



Thanks!!!!