Optimality and Stochasticity in Biological Networks

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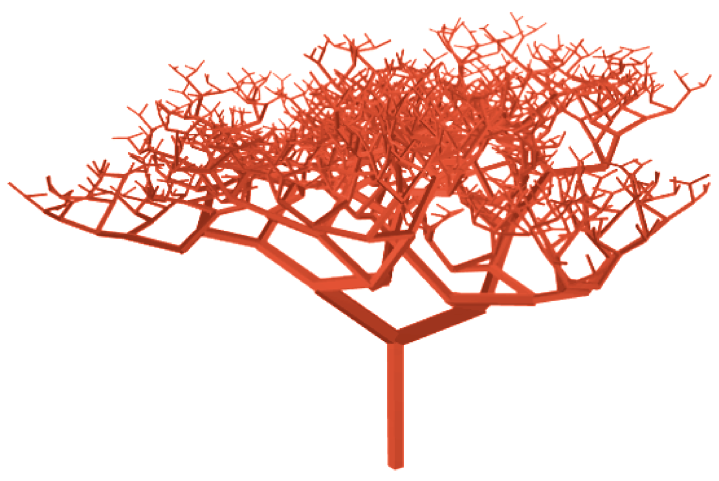
Introduction

Distribution networks in humans, animals and plants, despite showing an inherent randomness, are usually highly hierarchical and organised. Their roles are crucial and natural selection might have brought them to a certain level of optimality in accomplishing their functions. However, it is not completely clear yet how these complex networks reach their final structure and how they develop. Starting with a simple known example, the **binary homothetic tree**, here we present a framework capable of describing **branching morphogenesis** in mammalian organs and some of the efforts done in applying **optimal transport** to biological distribution networks. As two possible ways of exploring **biological contractile networks**, we apply optimal control theory to a 1D gland and we couple transport ideas with branching morphogenesis.

A simple example: The Binary Homothetic Tree

- Tree structure with 2^k new branches at generation k. N generations.
- At generation k all lengths are reduced by a factor h_k.
- Given a volume constraint and a uniform global flux, what $\mathbf{h} = (h_1, \ldots, h_N)$ minimizes power dissipation?



A shown in [1] the optimal tree turns out to be a **fractal tree** with h_1 depending on the volume constraint and constant $h_i = (1/2)^{1/3}$ for $i \geq 2$. Fractal dimension can be calculated as $\lim_{n\to\infty} \frac{\log 2}{\log 1/h_n} = 3$.

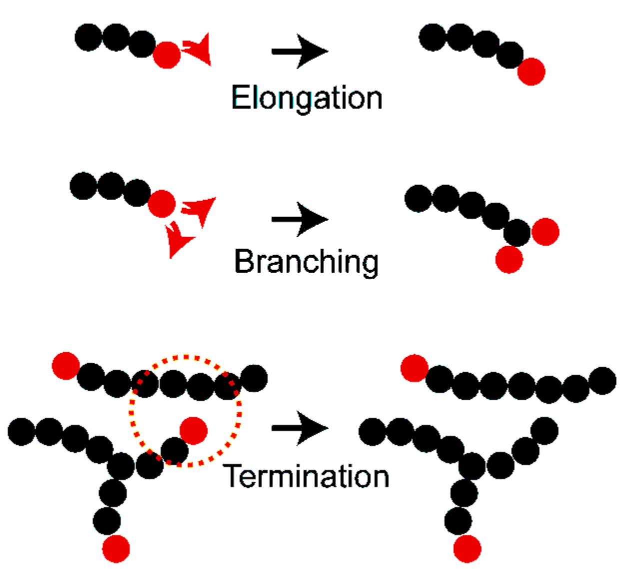
- $h < (1/2)^{1/3}$ makes the pressure drop divergent with N.
- $h > (1/2)^{1/3}$ means that the volume is larger than necessary and the total resistance of the network is smaller than in the optimal case.

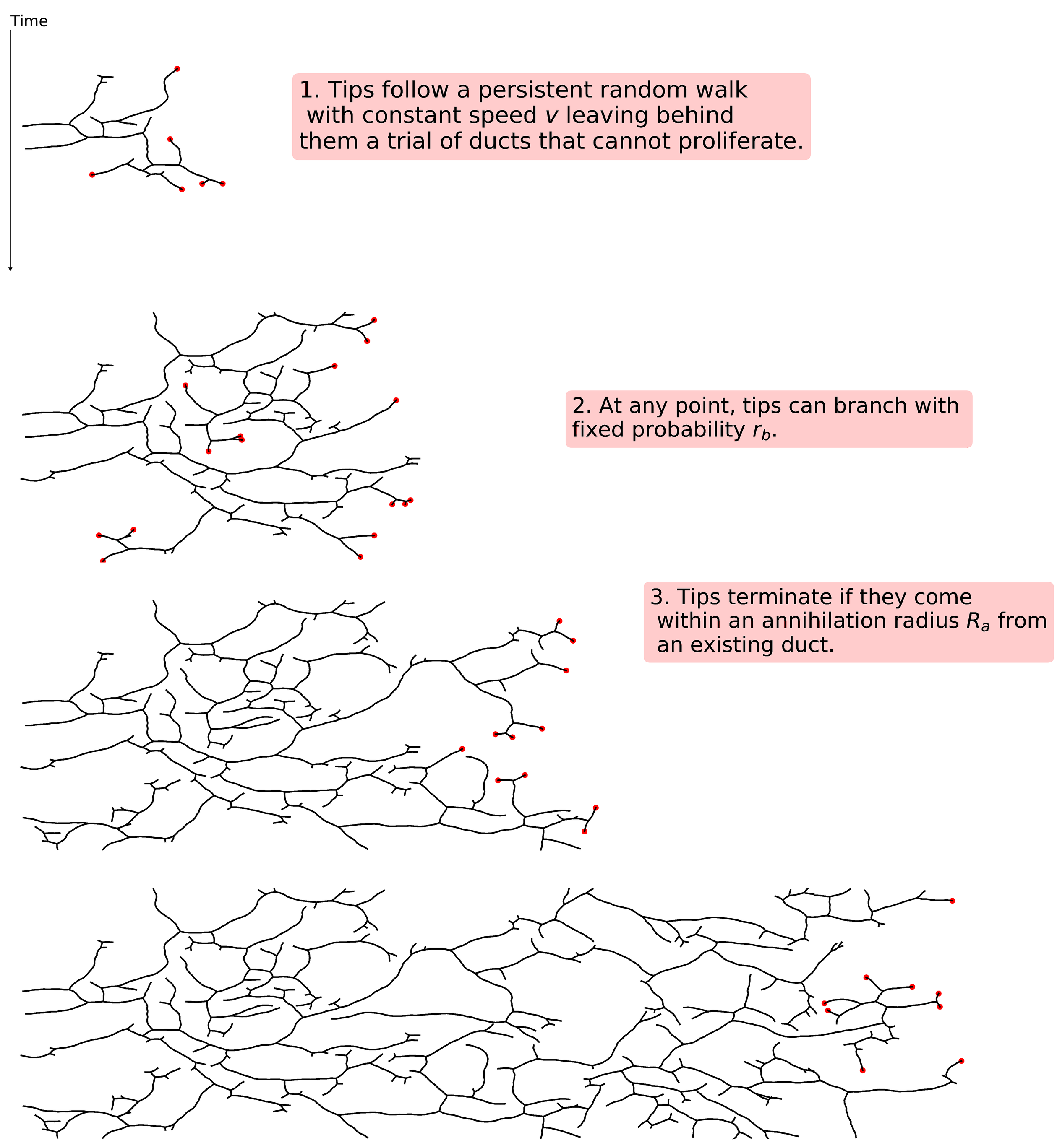
Remarkably, most mammalian lungs show $h \sim 0.85$ which gives a safety margin for breathing in bronchial constriction and being too close to the optimal value could be dangerous.

Branching morphogenesis

Branching morphogenesis in mammalian organs might follow the rules of **branching and annihilating random walks** (BARWs). In [2] it is shown that the topological features of mouse mammary gland, kidney, and human prostate can be explained by this framework.

BARWs from three rules





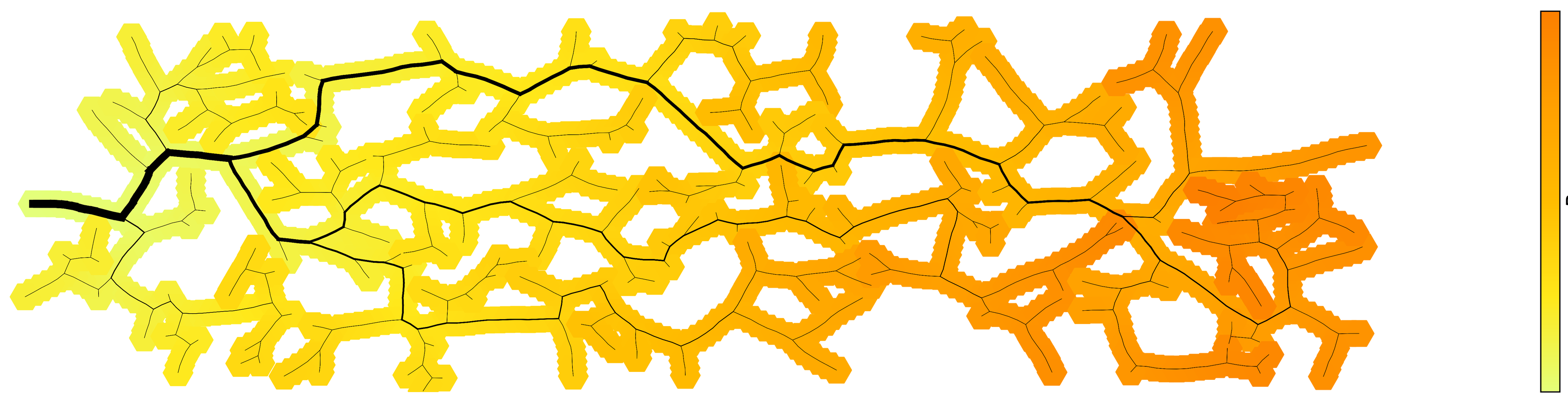
Morphogenesis follows from the activity of several tips that **randomly** explore the space and neutrally compete with each other, being annihilated when they are in proximity with other tips.

- Networks coming from stochastic growth are not necessarily **optimal**. Can we optimize these networks?
- Some distribution networks present **loopy structures** - e.g. the vascular system. These loops could contribute to network robustness in the presence of natural perturbations - [3].

Transport networks

Power dissipation functionals in complex networks usually present several local minima that can perform significantly worse than the global minima. Here, we use the adapation rule in [4] to optimize networks given some quantities that flow through them.

- Network compound by a set of edges and nodes.
- Flow follows **Poiseuille's law** and assume uniform source. Duct width is optimized.
- Assume network given by BARWs with persistence length $\to \infty$ and pressure nor conductivity have no effect on growth.



- After the optimization the network is **highly hierarchical**, usually with a few central ducts of high conductivity. Eventually they branch into thinner ducts that fill the available space. If coupled with stochastic growth, this hierarchy could translate into variable speed random walkers.
- If the network contains loops and the ingoing flow remains uniform, these loops tend to disappear with the optimization in order to avoid redundance. However, it has been shown that **loopy structures** emerge when bonds are broken or when there are **fluctuations** in the source - [3].

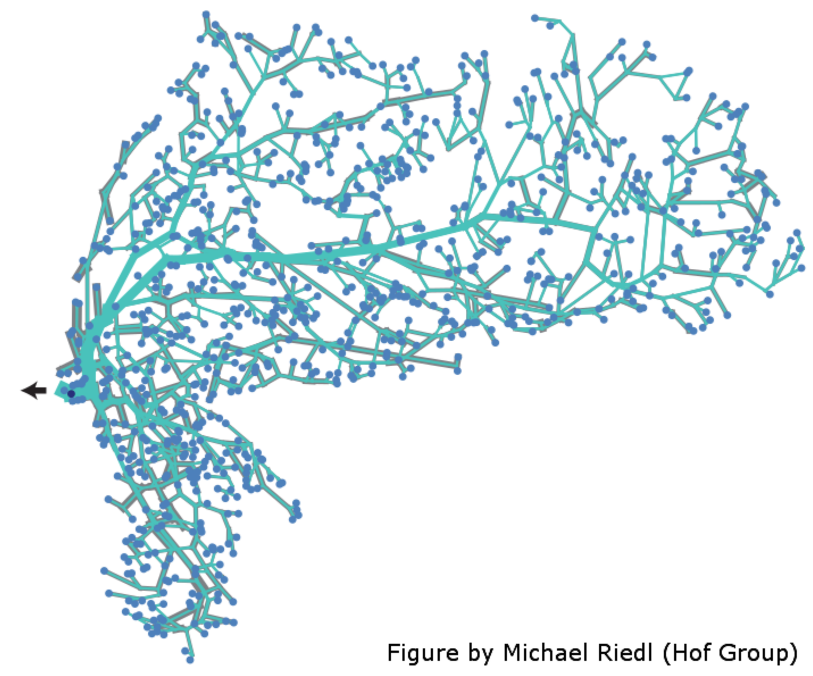


Figure by Michael Riedl (Hof Group)

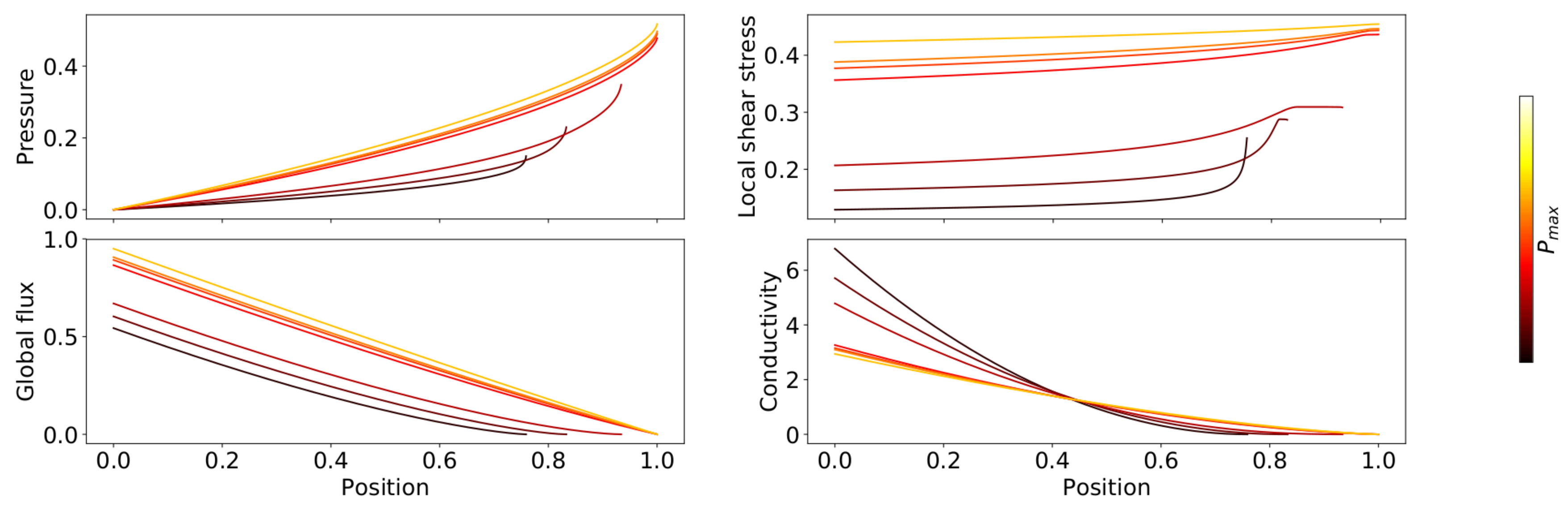
Transport in biological contractile networks

Some distribution networks have several **source inlets** whose flow are pressure-dependent. These inlets can be imagined as small alveoli with spheric shape and when they are constricted due to pressure, their ingoing flow can be reduced. They can even stop contributing to the network if the **pressure drop** is too large. These pressure-dependent effects could also affect to network growth.

Mean-Field calculations for a 1D gland

- System describing **1D glands**, with constant and continuous density of inlets.
- Flow follows **Poiseuille's law**.
- Inlets produce an ingoing flow that deppends on pressure $\propto 1 - \frac{P}{P_{\text{max}}}$, being P_{max} the threshold value from which inlets stop working.

Using **Optimal Control Theory** one can find the conductivity of the gland as a function of space that minimizes power dissipation under some material constraint.

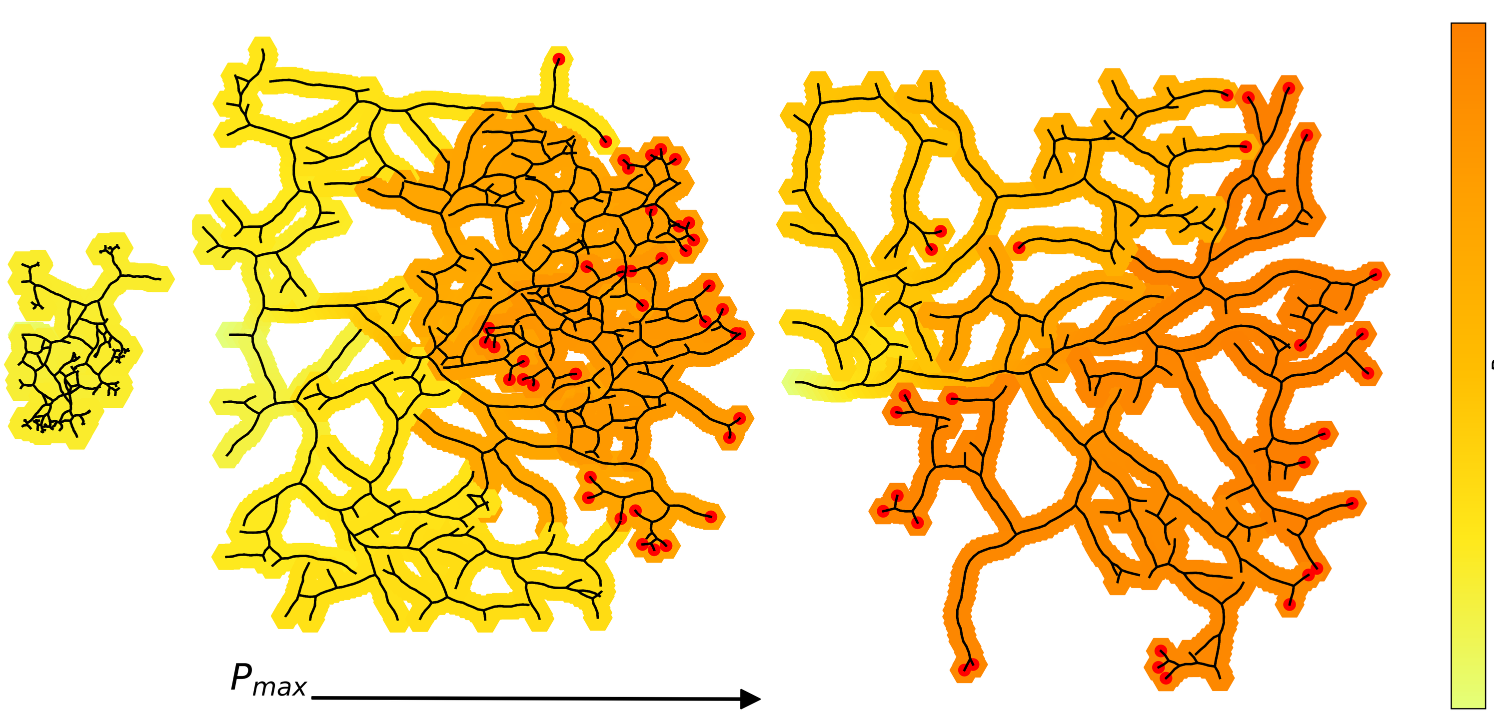


Results show **two different behaviours** deppending on the magnitude of P_{max}. These become evident in stress and global flux plots. Whenever a small P_{max} causes the gland to terminate earlier, stress shows a sudden increase near the end and **total outflow** is far from the ideal non-contractile case outflow.

BARWs in contractile trees

From a biological point of view, tip termination could be a complicated process. Tips might been designed to terminate within some time interval or whenever their environment satisfied some specific properties.

Using the BARW framework, we explore the effects of pressure on the random walkers speed assuming all lengths are reescaled by a factor $1 - \frac{P}{P_{\text{max}}}$. When tips reach P_{max} they terminate.



References

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[4] H. Ronellenfitsch and E. Katifori. Global Optimization, Local Adaptation, and the Role of Growth in Distribution Networks. *Phys. Rev. Lett.* 117, 138301 (2016)