Structure and dynamics of endoplasmic reticulum networks

dynamics reading group

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Biological background

The ER is the largest membrane-bound organelle and spreads throughout the cytoplasm as one highly **complicated interconnected** network.

It serves important roles in protein synthesis, calcium storage, ect.

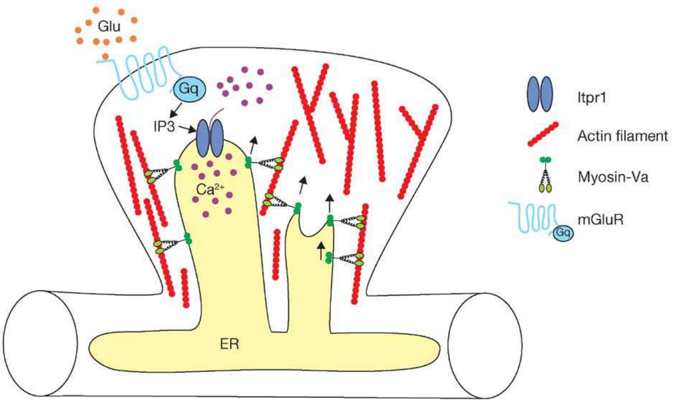

Image is taken from Stiess, M and Bradke, F. *Nature Cell Biology* 13:10-11(2011).

Biological background

The ER network in a tobacco leaf epidermal cells (Sparkes2009)

control condition latrunculin B treated condition

ER structure is composed of tubules and cisternae.

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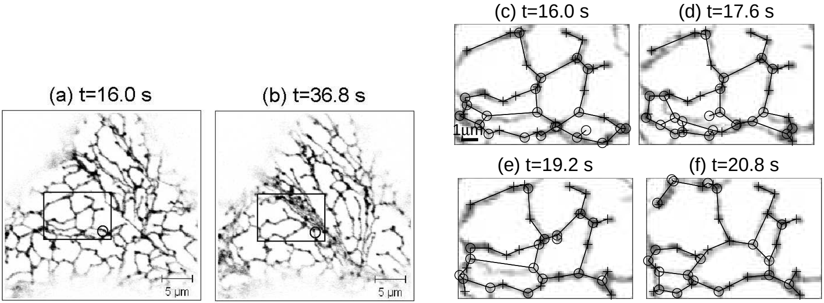
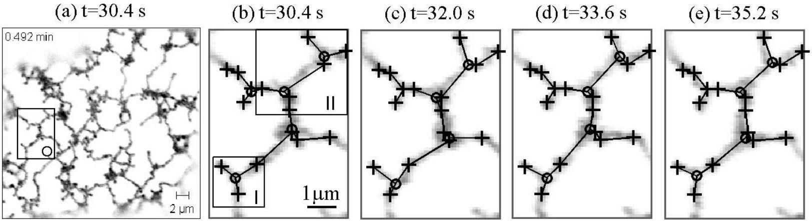
Geometry graph representation

control ER



treated ER



Euclidean Steiner Network

A Steiner tree (ST) is a tree whose length cannot be shortened by a small perturbation of Steiner points, even when splitting is allowed (Gilbert and Pollak 1968).

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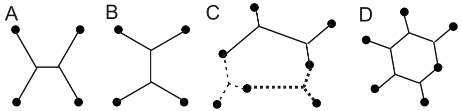
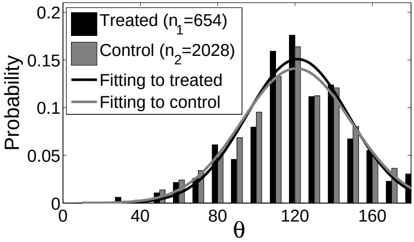
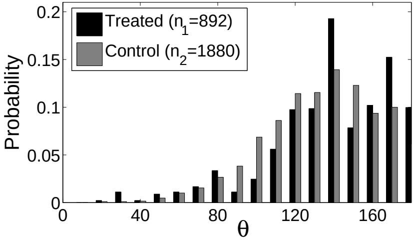
We say G is an Euclidean Steiner network (ESN) between these terminals (and the additional points are Steiner points) if no small perturbation of Steiner points will decrease the length, even if splitting is allowed



Instantaneous ER network analysis
Angle distribution

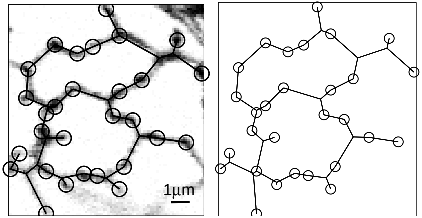




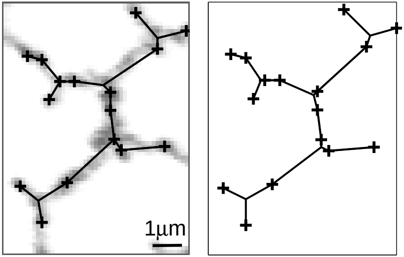
Instantaneous ER network analysis

ER network vs ESN

control



treat



These suggest that the ER networks are well modelled as perturbed ESNs.

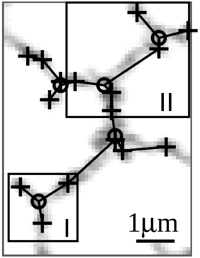
ER dynamics in treated condition

We model the motion of non-persistent nodes (junctions in the ER) $x_i(t) \in R^2$ for $i = 1..M$ as

$$\dot{x_i} = -a\nabla_{x_i} f(x_i, \ldots, x_P) + \sqrt{2\sigma}\xi(t) \quad (1)$$

$f(x_i, \ldots, x_P)$: the total length of a graph
a (unit $\mu m/s$): a drift coefficient
σ (units $\mu m^2/s$): a diffusion coefficient modulating white noise $\xi(t)$: with zero mean and autocorrelation $\langle \xi(t)\xi(t')\rangle = \delta(t - t')$.

(b) t=30.4 s



ER dynamics in treated condition

Parameter Estimation for Region I

Estimation of diffusion coefficient: via quadratic variation $\langle X, X \rangle_t := \lim_{||P|| \to 0} \sum_{k=1}^{n} |X_{t_k} - X_{t_{k-1}}|^2$ where P ranges over partitions of the interval $[0, t]$ and the norm of the partition P is the mesh.

$$\sigma \approx \frac{1}{2Nd\,\delta} \sum_{n=1}^{N-1} |x((n+1)\delta) - x(n\delta)|^2 = 0.008 \mu m^2/s \qquad (2)$$

ER dynamics in treated condition

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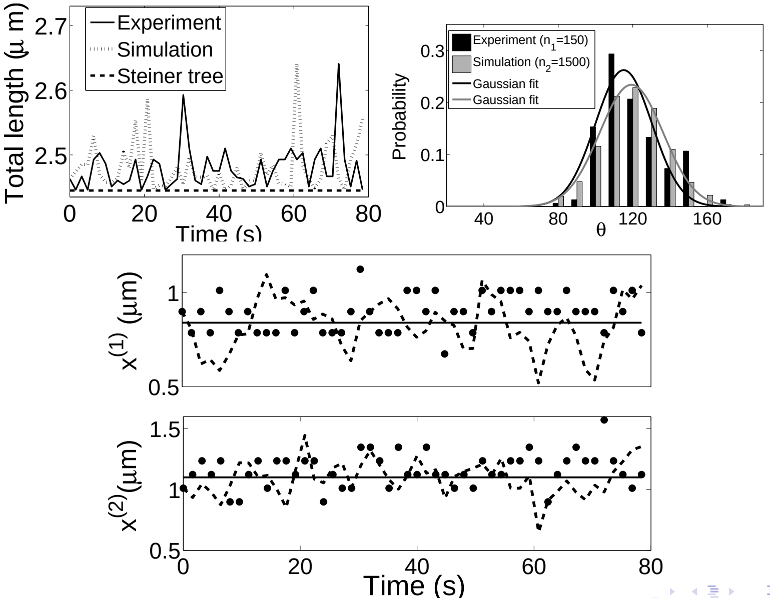
Estimation of drif coefficient: via maximizing approximated log likelihood function $\mathcal{L}(\theta|x) = P(x|\theta)$.

$$a \approx -\frac{\sum_{n=1}^{N-1} \langle \nabla f(x(n)), (x(n+1) - x(n)) \rangle}{\sum_{n=1}^{N-1} \delta |\nabla f(x(n))|^2} = 0.2\mu m/s \qquad (3)$$

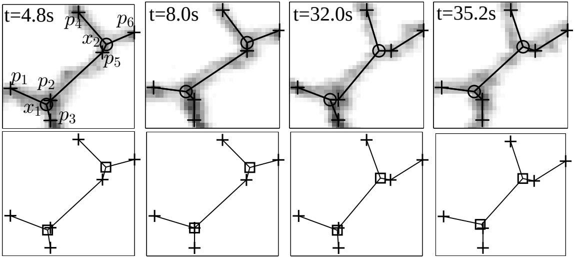
ER dynamics in treated condition

Region I (experimental vs simulation results)



ER dynamics in treated condition

Region II



ER dynamics in treated condition

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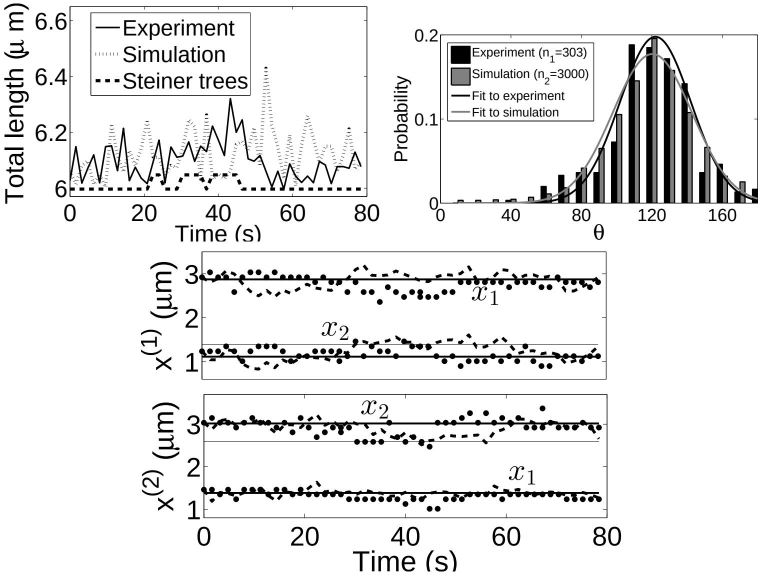
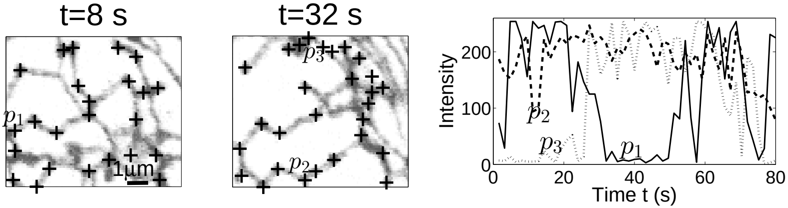


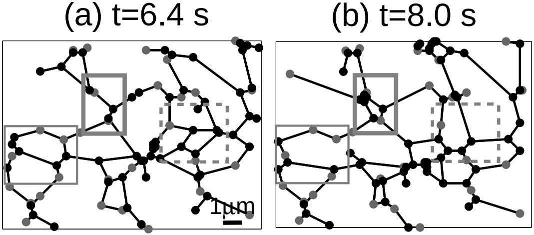
ER remodelling in the control

the dynamics of the control ER network is much richer

persistent node characterization



complex structural changes



Physical quantities estimation

A number of assumptions:

A1 the ER filaments are approximately cylindrical with constant radius R and surface tension γ; this means that the tension force $F := 2\pi R\gamma$ is approximately constant in the ER filaments.

A2 the environment outside the ER filament is fluid with constant effecitive viscosity η.

A3 the ER junction can be approximated as a sphere of radius R that is acted on purely by Stokes drag, filament tension and Brownian forces.

Physical quantities estimation

For Region I, the non-persistent node $x(t) \in R^2$ moves so that the tension and Stokes drag forces balance the Brownian forces; hence x satisfies the Langevin equation

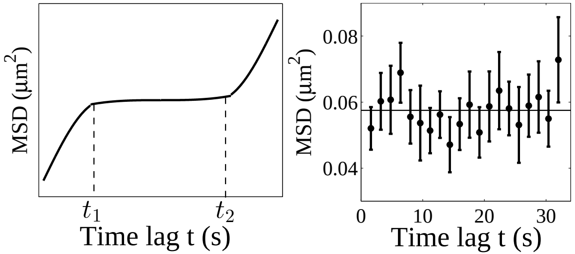
$$F\nabla_x f(x) + 6\pi\eta R\dot{x} = \sqrt{2k_B T 6\pi\eta R}\xi(t). \tag{4}$$

This reduces to Eq (1) with $a = \frac{F}{6\pi\eta R}$ and $\sigma = \frac{k_B T}{6\pi\eta R}$. The ER filament diameter $D := 2R = 0.06\mu m$ (Shibata,Y *et al* 2009); temperature $T = 298K$. This relations gives

$$\eta \approx 909cP \text{ and } F \approx 0.1pN$$

Physical quantities estimation

The cytoplasm displays both elastic and viscous characteristics (Tseng, *et al* 2002)



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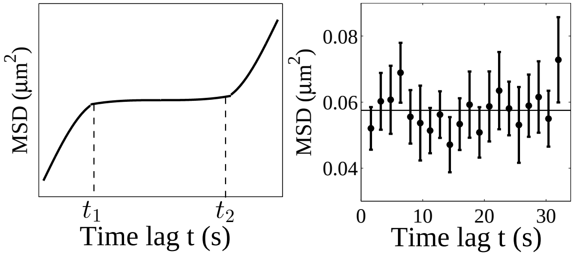

This indicates that at this time scale, the cytoplasm behaves predominantly elastic and the effective viscosity $\eta = 909cP$ is an overestimation of local cytoplasm viscosity.

Thanks