Kavli IPMU - RIKEN iTHES - Osaka TSRP
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Synchronizing Biological Oscillators with Active Movement

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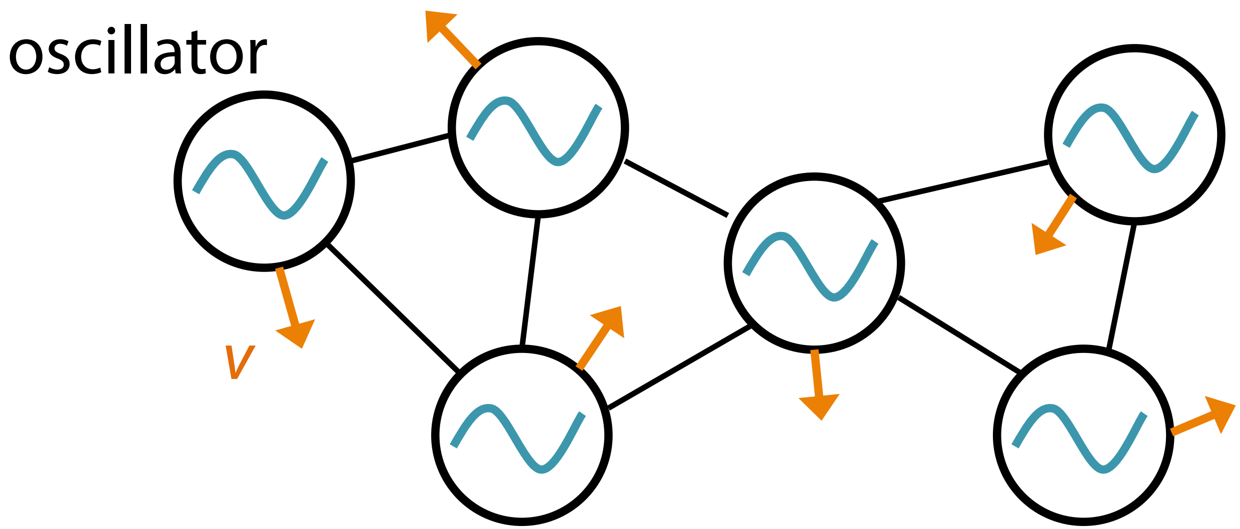
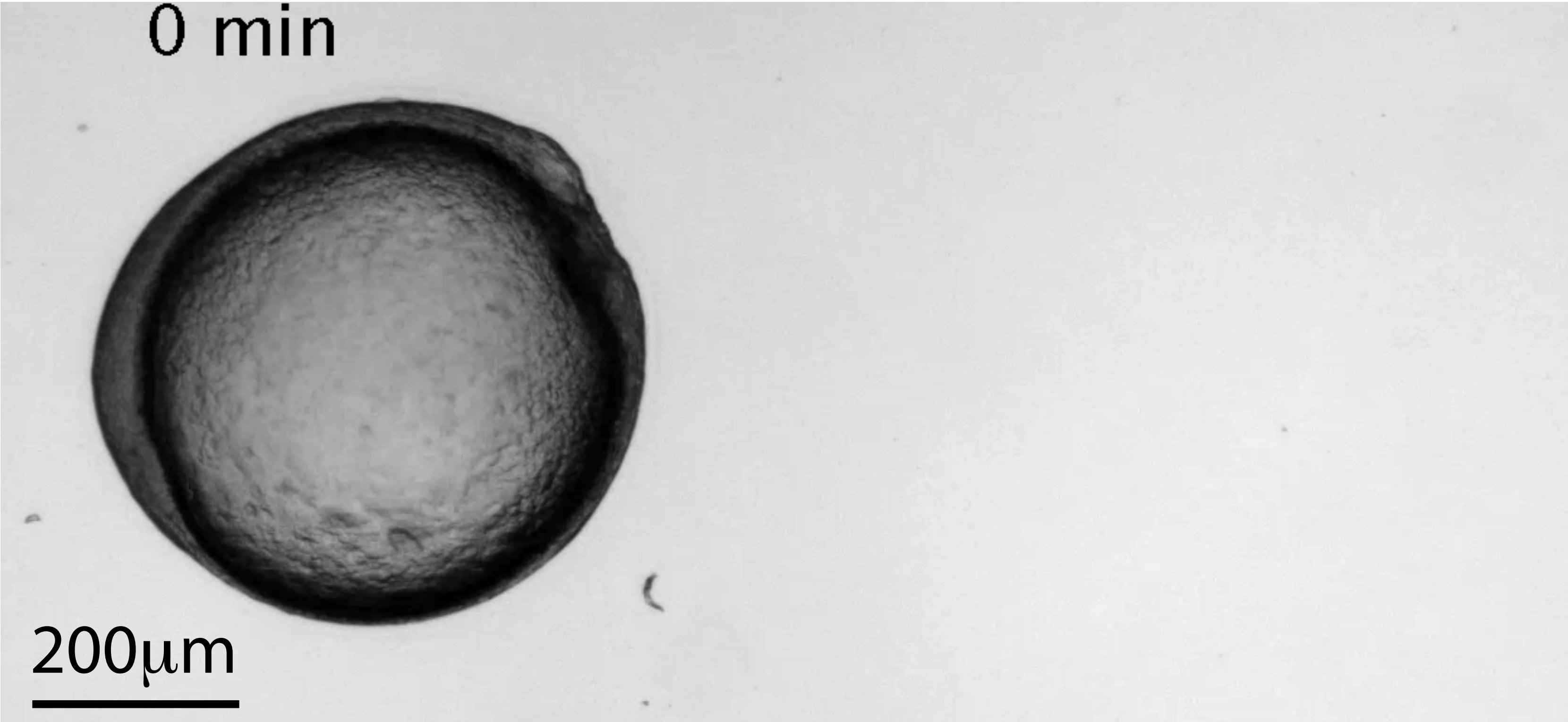
Topic

Synchronization of **mobile**, locally coupled oscillators



How the mobility of oscillators changes synchronization dynamics?

Formation of a segmental body

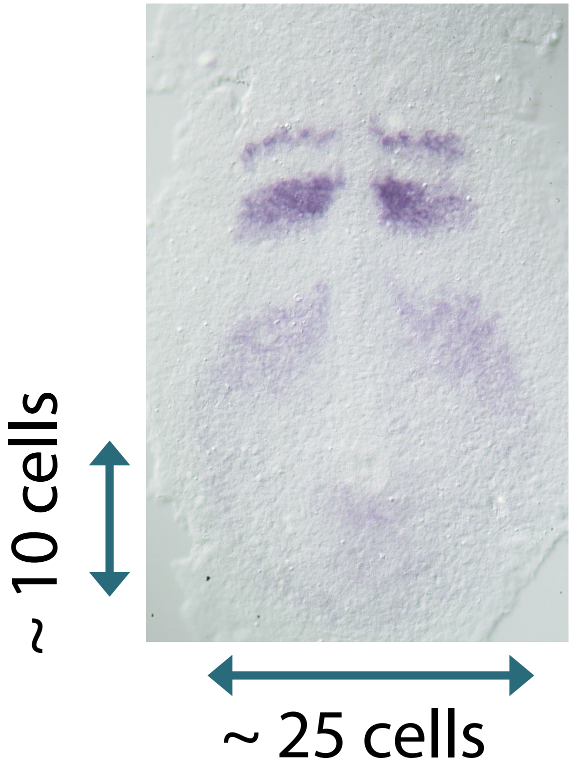


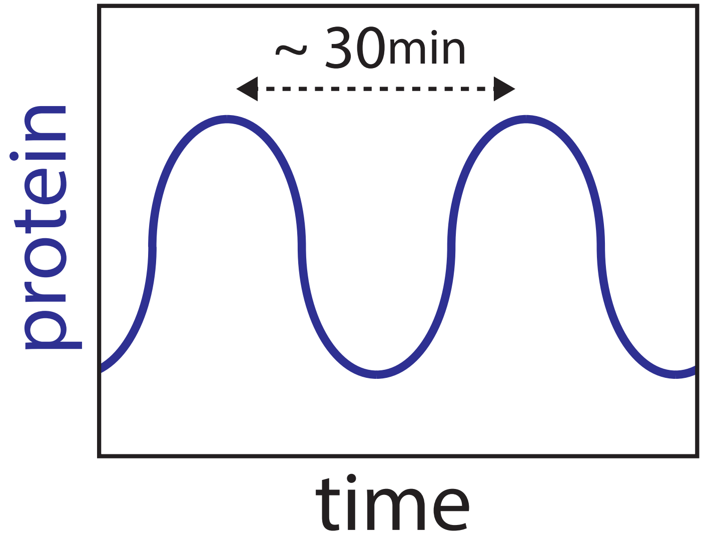
cell diameter ~ 10μm
segment size ~ 50μm

Segmentation occurs rhythmically

Schröter et al. 2008 Dev. Dyn.

Synchronized protein oscillation





period ~ 30 min

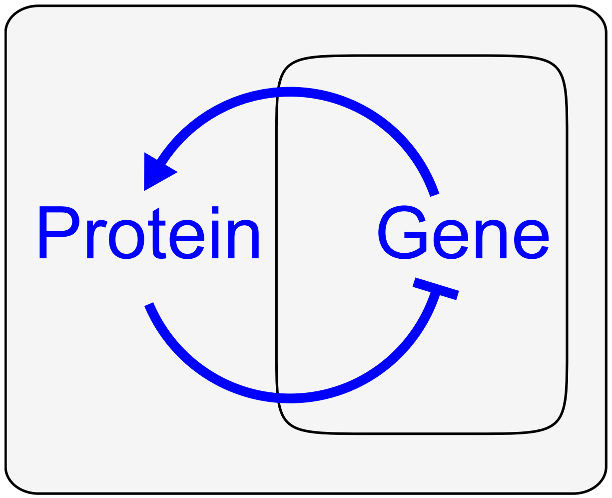
Protein concentration oscillates inside cells

Oscillation is synchronized across a population of cells

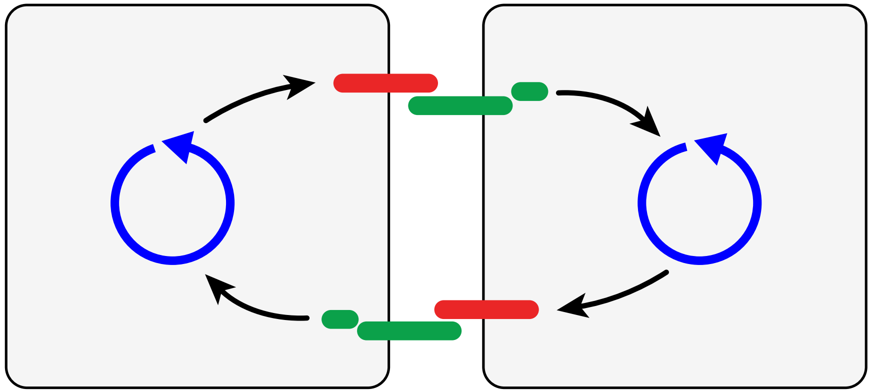
Oates et al. 2009 Nat. Rev. Genet.

Locally coupled Biological oscillators

Sustained oscillation by negative feedback

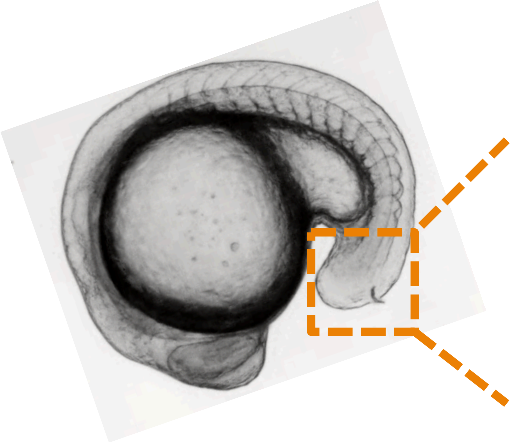


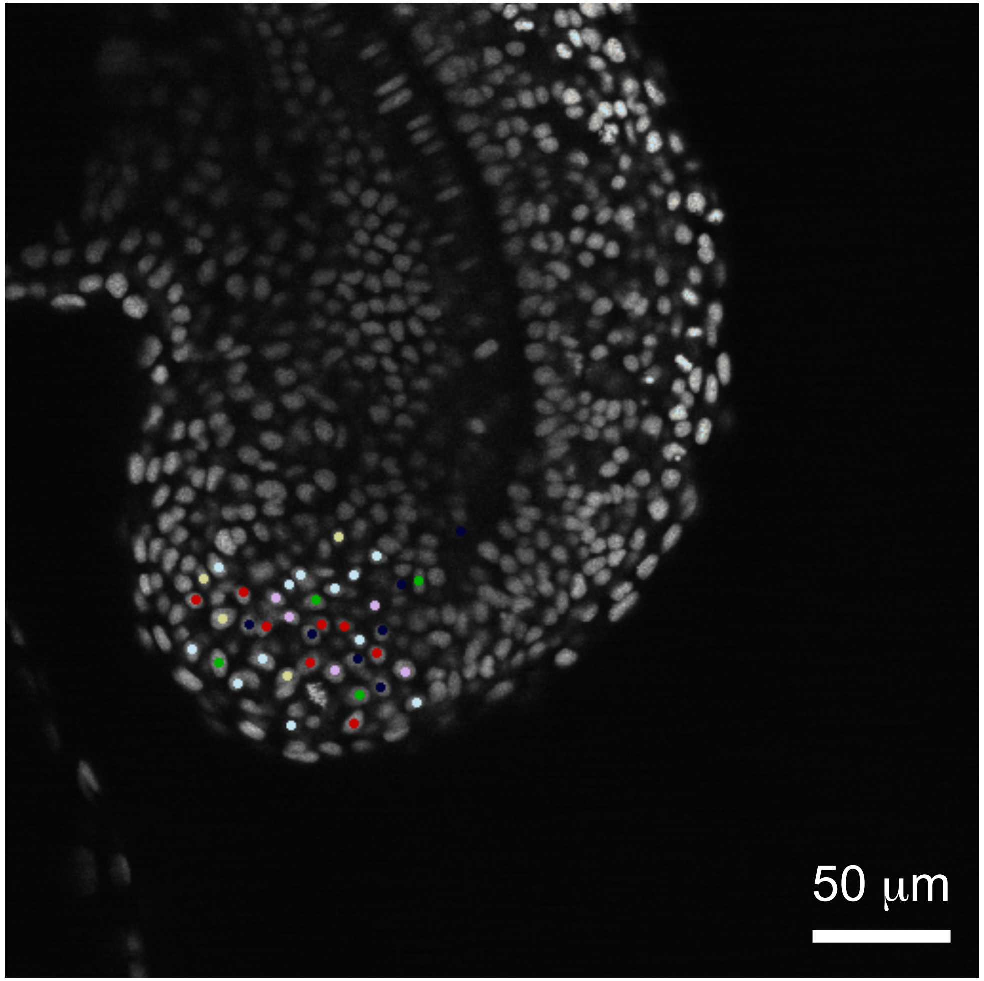
Nearest neighbor coupling via membrane proteins



Oates et al. 2012 Development

Cell movement in the tissue





white dot:
cell nucleus

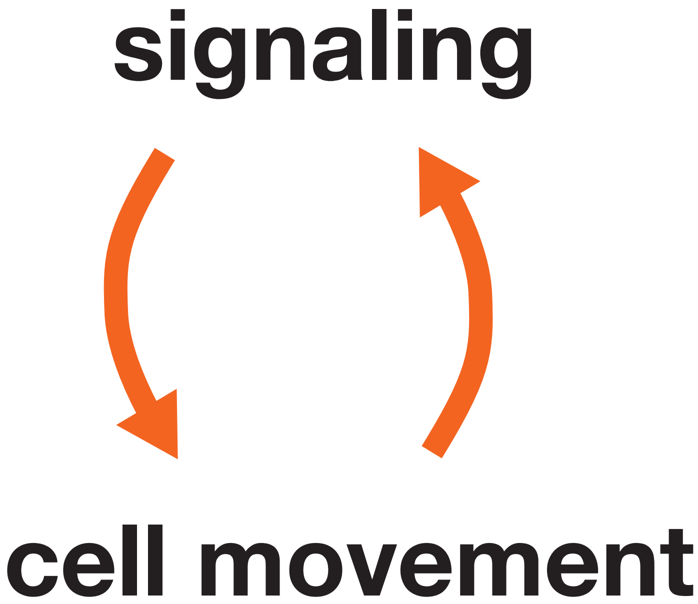
Movement causes the exchange of neighboring oscillators

movie by Bhavna Rajasekaran

Question

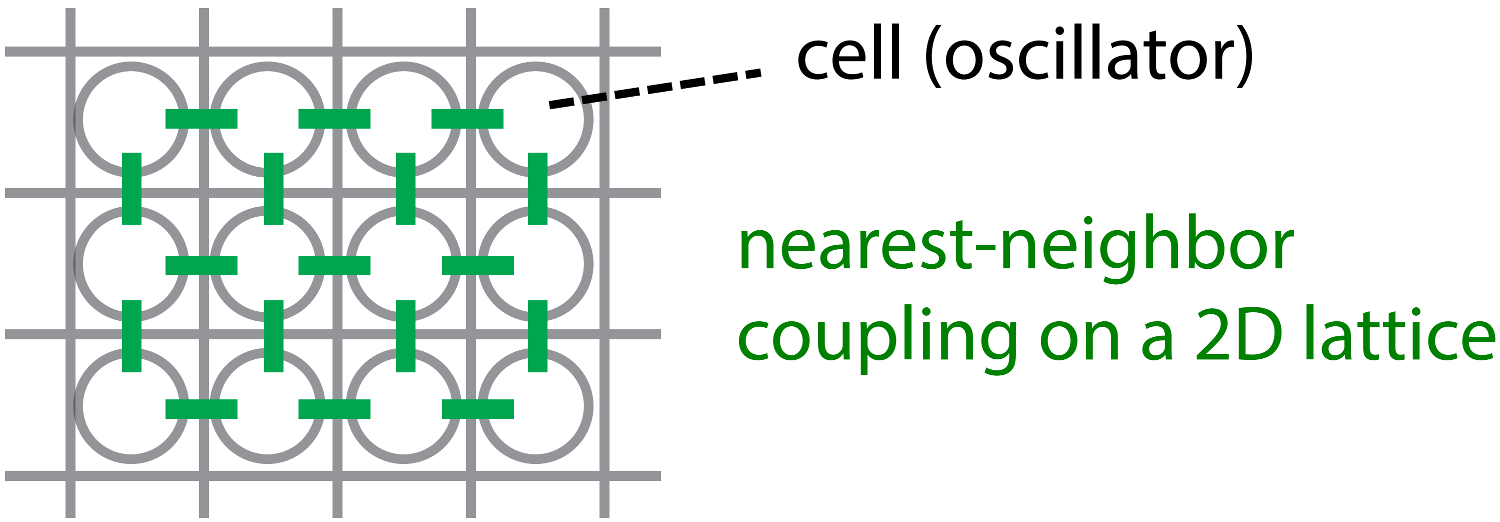
How does movement affect synchronization?

Cell signaling and movement are common in Biology

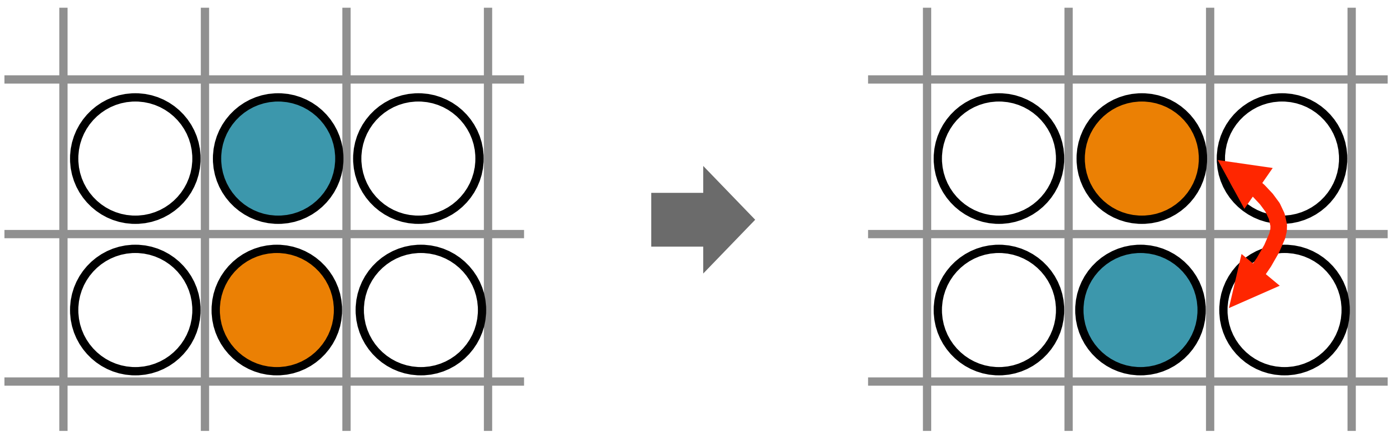


Understanding this Interplay would be fundamental

Movement as the exchange of locations



Random walk of oscillators



Regulation of protein concentration

her 1:

$$\frac{dm_{h1}^{(j)}(t)}{dt} = k\frac{1+\overline{p}_D^{(j)}(t-T_{h1})/\overline{p}_{0D}}{1+\overline{p}_D^{(j)}(t-T_{h1})/\overline{p}_{0D}+\left(p_{H1}^{(j)}(t-T_{h1})/p_{0H}\right)\left(p_{H7}^{(j)}(t-T_{h1})/p_{0H}\right)} - c_{h1}m_{h1}^{(j)}(t)$$

her 7:

$$\frac{dm_{h7}^{(j)}(t)}{dt} = k\frac{1+\overline{p}_D^{(j)}(t-T_{h7})/\overline{p}_{0D}}{1+\overline{p}_D^{(j)}(t-T_{h7})/\overline{p}_{0D}+\left(p_{H1}^{(j)}(t-T_{h7})/p_{0H}\right)\left(p_{H7}^{(j)}(t-T_{h7})/p_{0H}\right)} - c_{h7}m_{h7}^{(j)}(t)$$

delta:

$$\frac{dm_{d}^{(j)}(t)}{dt} = \frac{k}{1+\left(p_{H1}^{(j)}(t-T_{d})/p_{0H}\right)\left(p_{H7}^{(j)}(t-T_{d})/p_{0H}\right)} - c_{d}m_{d}^{(j)}(t)$$

HER 1:

$$\frac{dp_{H1}^{(j)}(t)}{dt} = am_{h1}^{(j)}(t-T_{H1}) - bp_{H1}^{(j)}(t)$$

HER 7:

$$\frac{dp_{H7}^{(j)}(t)}{dt} = am_{h7}^{(j)}(t-T_{H7}) - bp_{H7}^{(j)}(t)$$

DELTA:

$$\frac{dp_{D}^{(j)}(t)}{dt} = am_{d}^{(j)}(t-T_{D}) - bp_{D}^{(j)}(t)$$

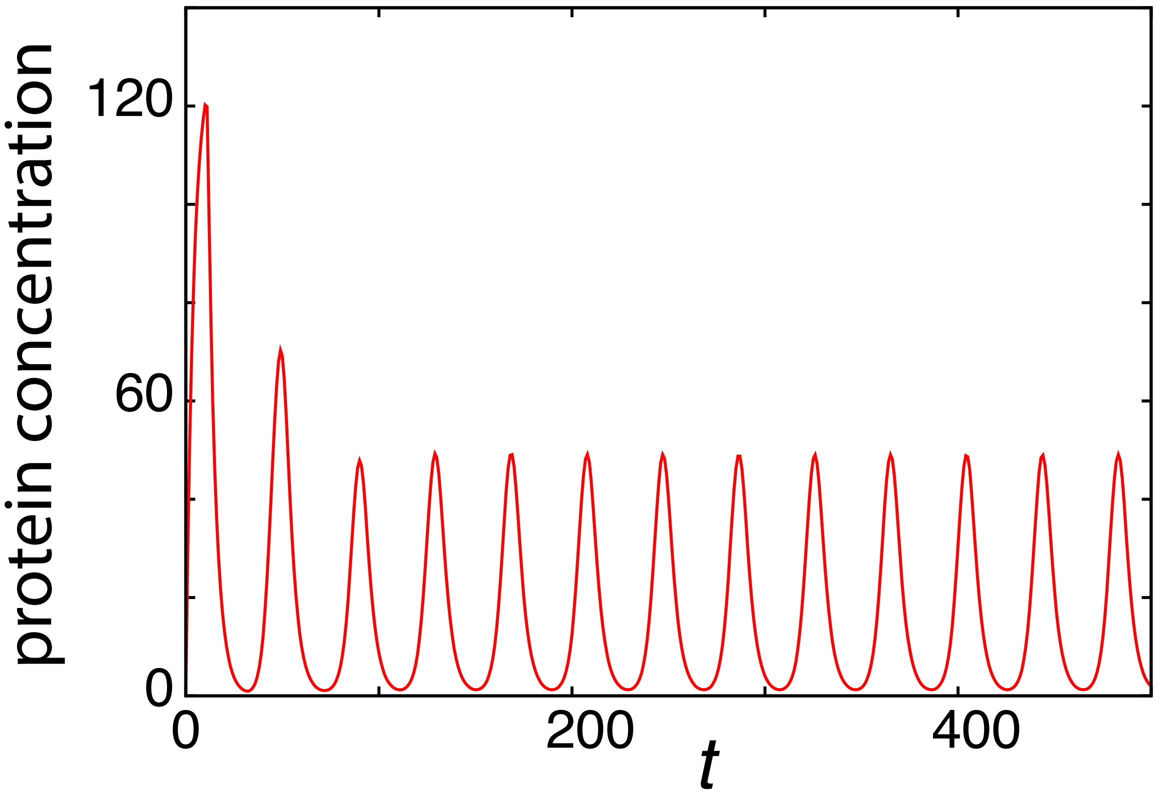
cellular oscillators
+
coupling

Details of equations are not important for the rest of my talk.

Lewis, 2003 Curr. Biol.

Limit cycle

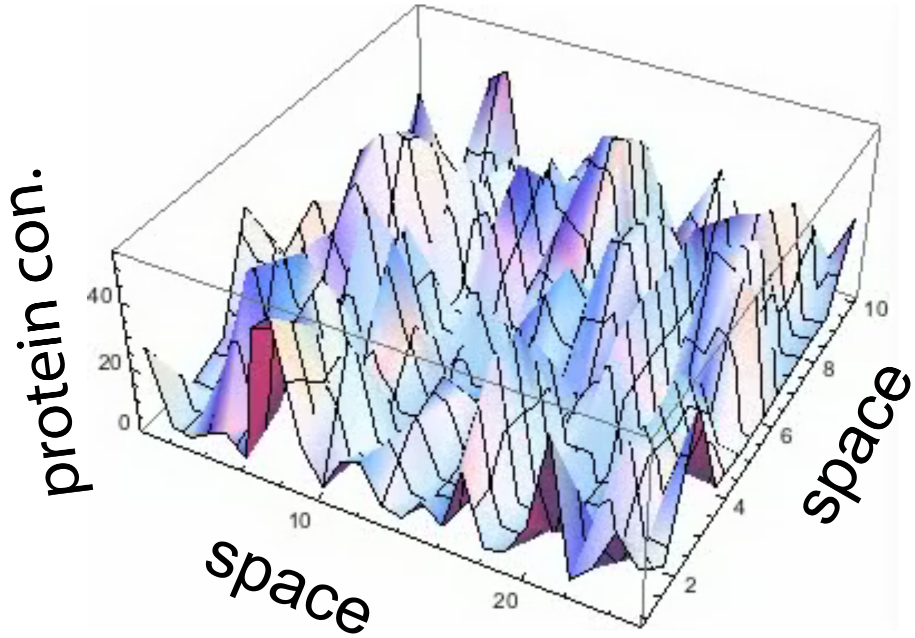
Numerical simulation for $N = 1$ (uncoupled cell)



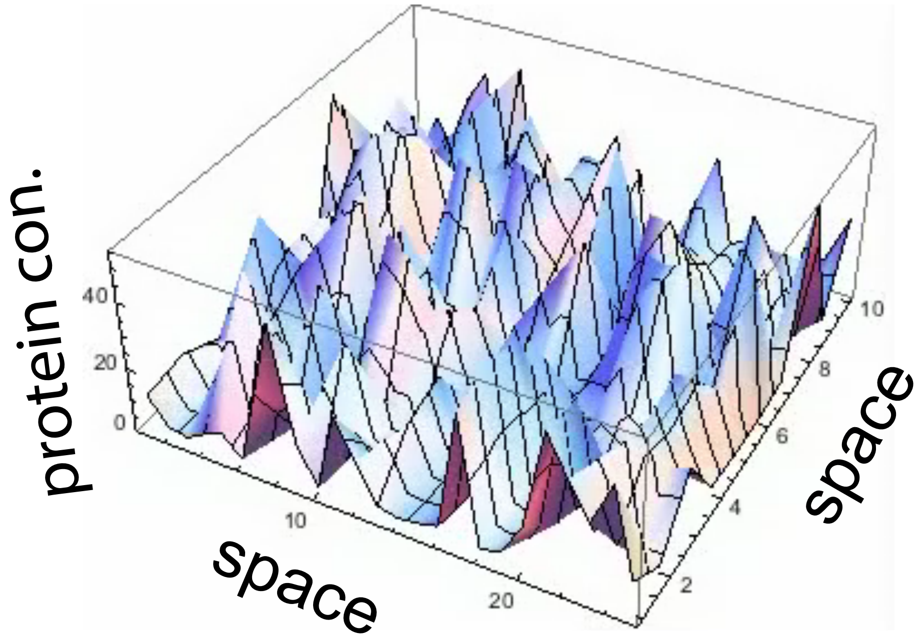
What happens when we couple many (but finite) of these oscillators in the presence of movement?

Simulations

withOUT movement



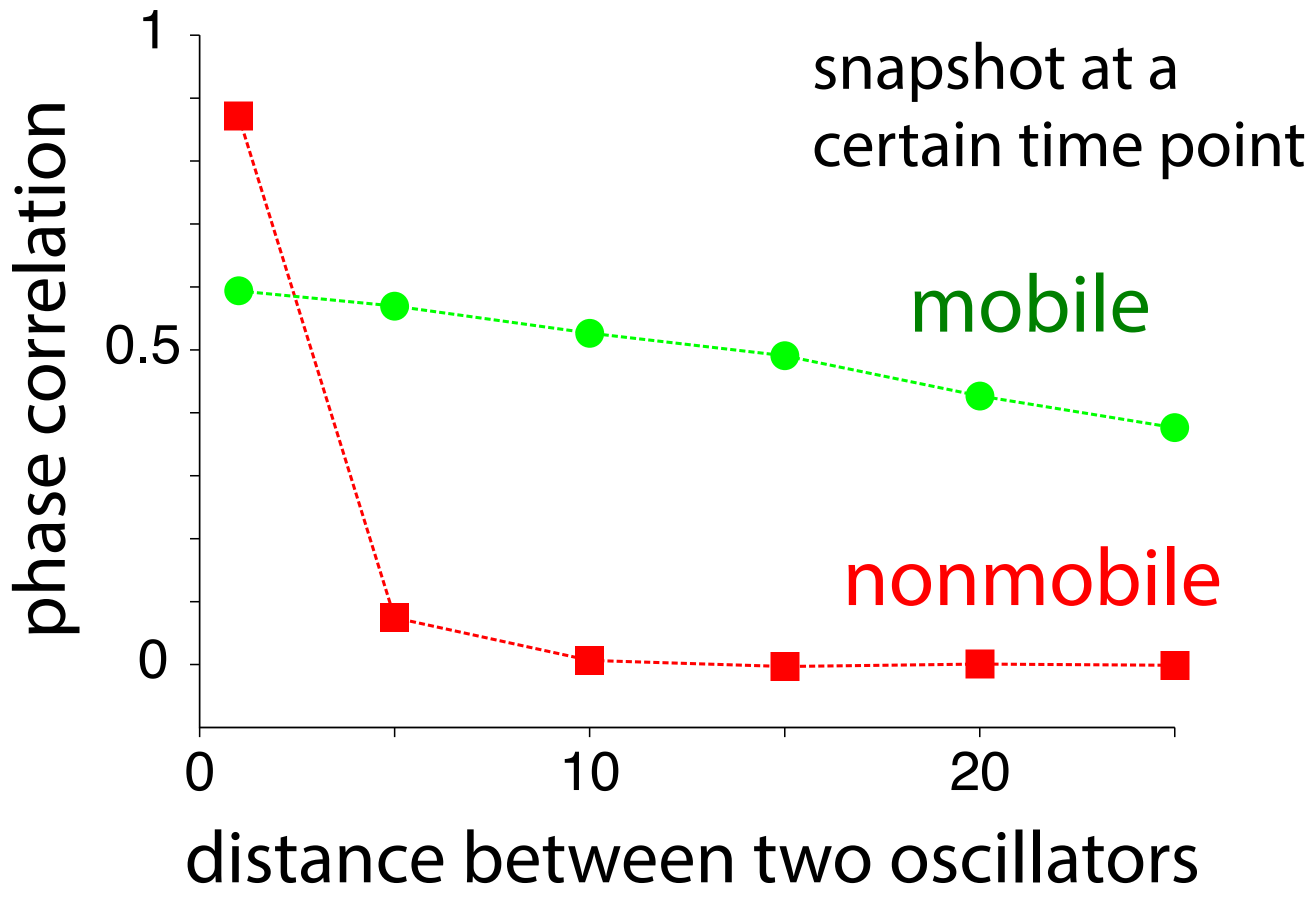
with movement



Movement enhances global synchronization

Uriu et al. 2010 PNAS

Phase correlation between two oscillators

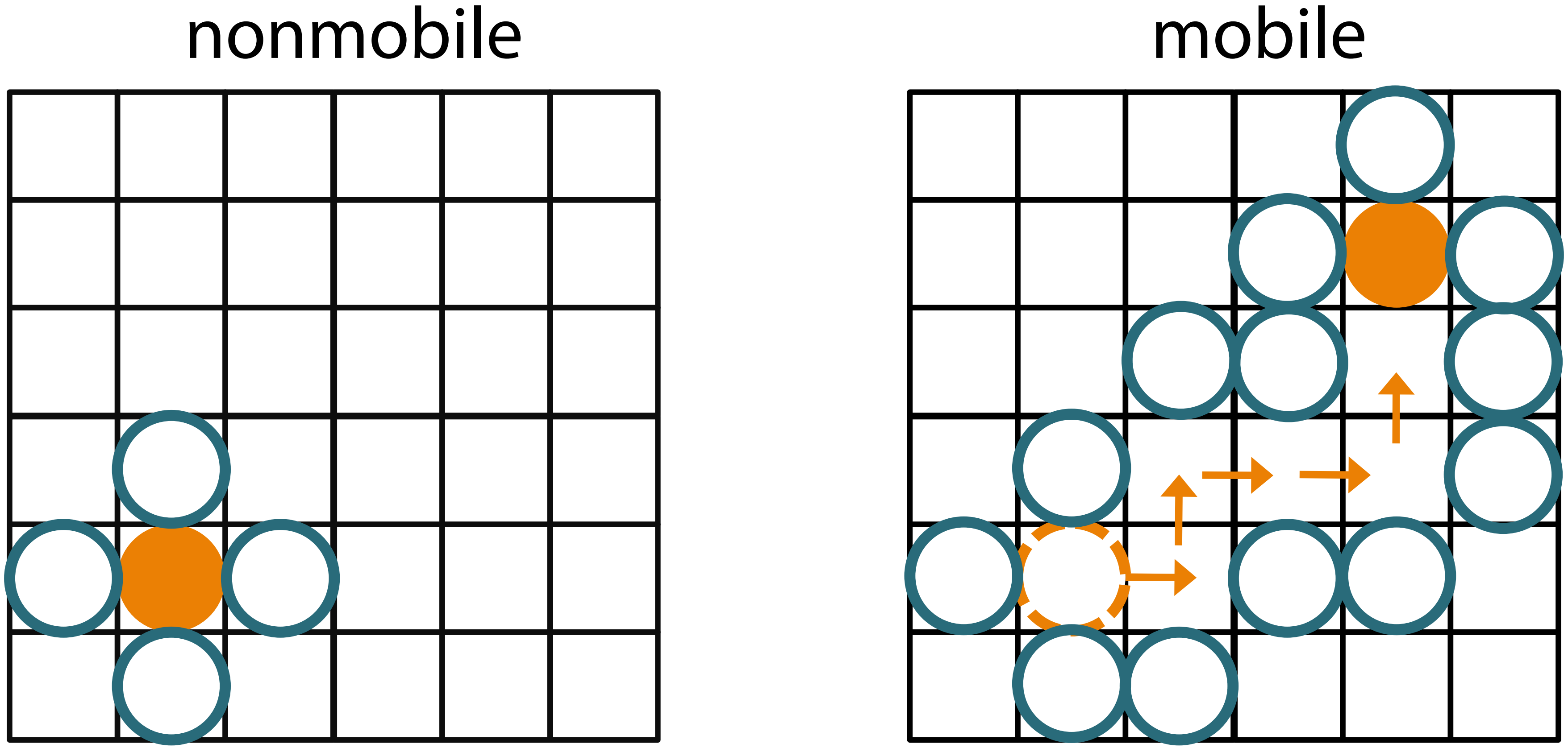


nonmobile higher local correlation, shorter lengthscale

mobile lower local correlation, longer lengthscale

Interaction range

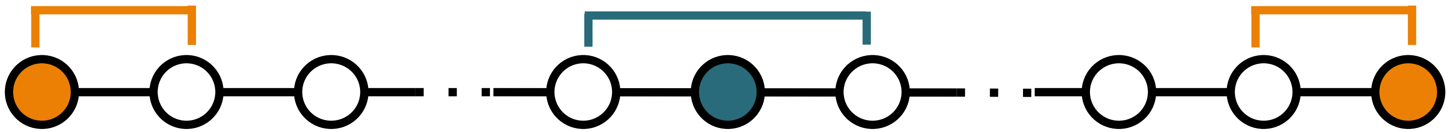
Mobility effectively extends interaction range



Can we write the interaction range?

Identical phase oscillators on a 1D chain

nearest neighbor coupling



phase of oscillator *j*

coupling strength

timescale for phase dynamics

$$\frac{d\theta_j}{dt} = \omega + \frac{\kappa}{n_j} \sum_{j'} \sin\left[\theta_{j'}(t) - \theta_j(t)\right]$$

intrinsic frequency

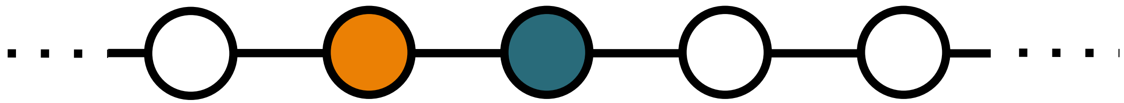
coupling

Kuramoto 1984
Sakaguchi et al. 1987

Oscillators always reach complete synchronization.

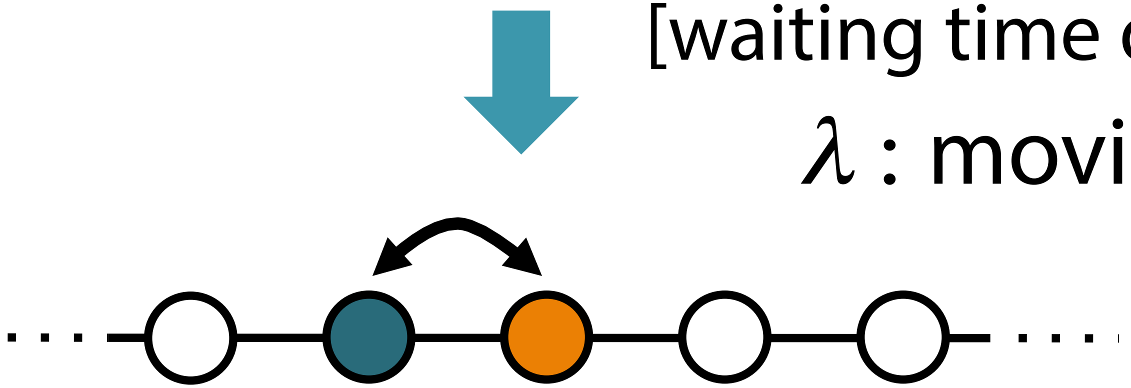
➡ How mobility changes transient dynamics?

Mobility of oscillators



[waiting time dist.] = $\lambda e^{-\lambda t}$

λ : moving rate



average waiting time = $1 / \lambda$

λ diffusion constant of oscillators

two timescales

phase dynamics ($1/\kappa$)

movement ($1/\lambda$)

Synchronization time T_c

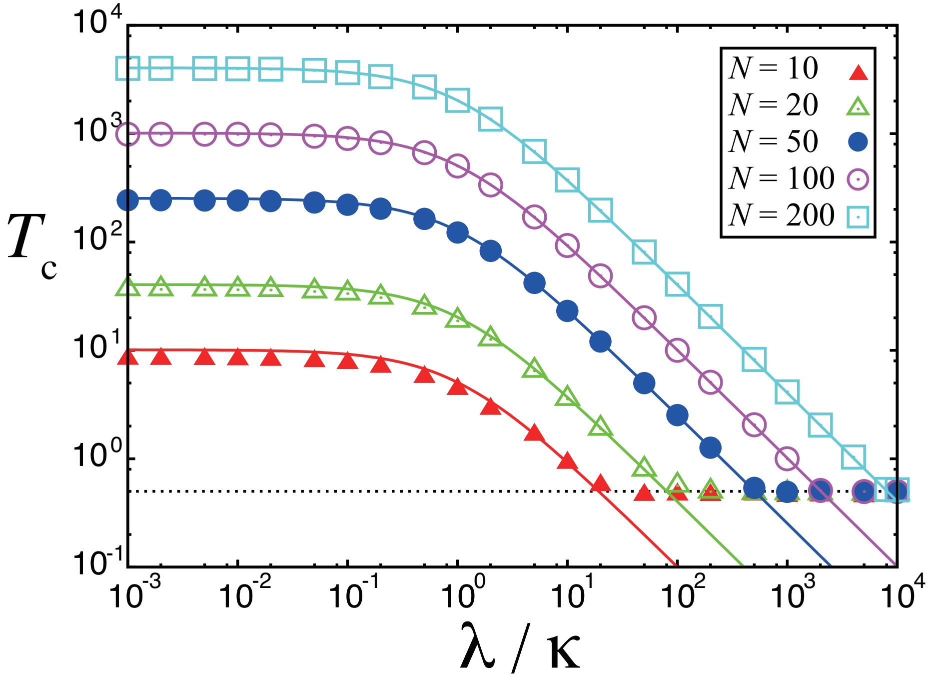
$$T_c \approx \frac{N^2}{\pi^2 \kappa} \frac{1}{1+\lambda/\kappa}$$

smaller T_c: faster attainment of synchronization

N total number of oscillators

κ coupling strength

λ moving rate



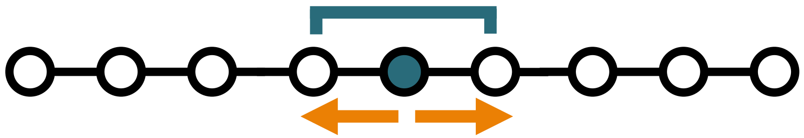
(dependence on λ with fixed κ)

symbols: simulations
lines: equation for T_c

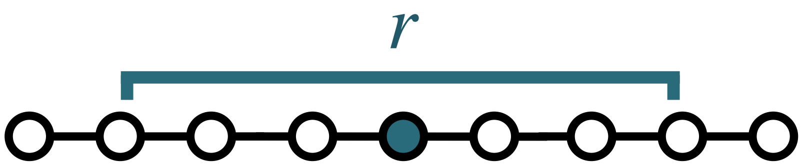
Uriu et al. 2013 Phys. Rev. E

Calculation of an effective interaction range

$T_c(\lambda/\kappa)$ mobile + nearest neighbor coupling

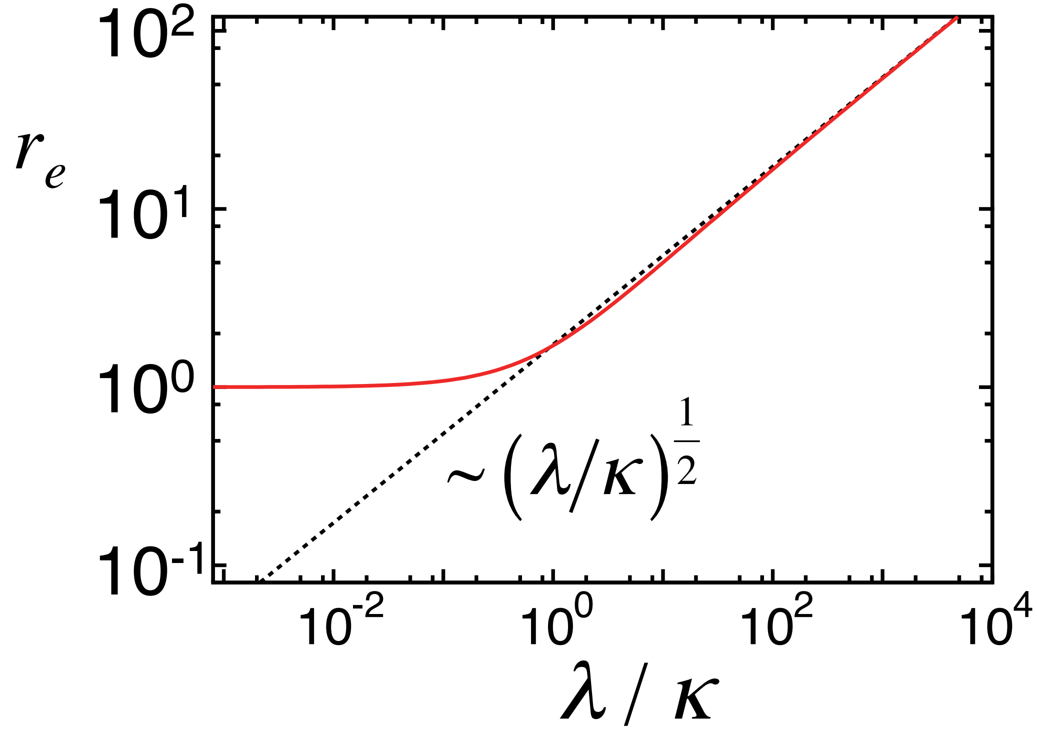


$T_c(r)$ nonmobile + long range coupling



Solve $T_c(r) = T_c(\lambda/\kappa)$ with respect to r

Interaction range extended by mobility



Effective interaction range r_e

$$r_e \approx \frac{-3 + 7\sqrt{1 + \lambda/\kappa}}{4}$$

when $\lambda/\kappa >> 1$

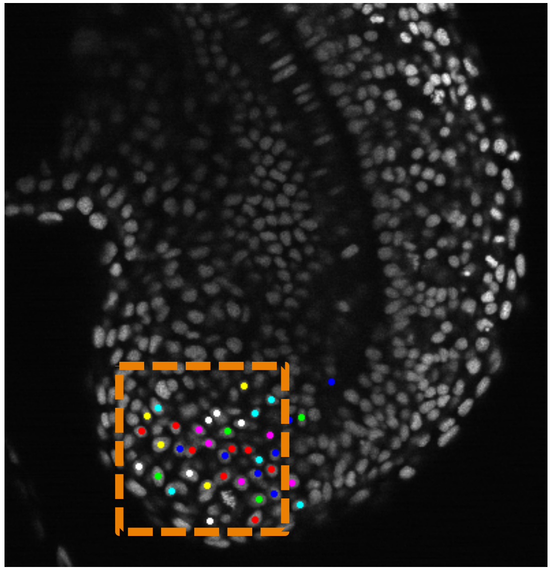
$$r_e \propto \sqrt{\lambda/\kappa}$$

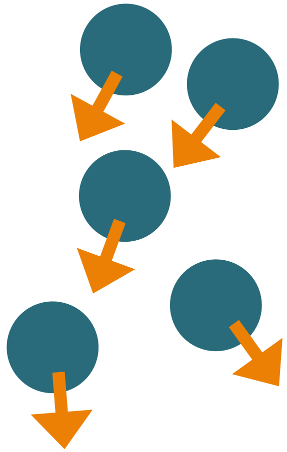
Root mean squared distance in time $1/\kappa$ with the diffusion constant λ

Uriu et al. 2013 Phys. Rev. E

Collective cell movement in the tissue

Positive correlation of direction of motion among cells





velocity correlation length

2~ 10 cell diameters

Lawton et al. 2013 Development

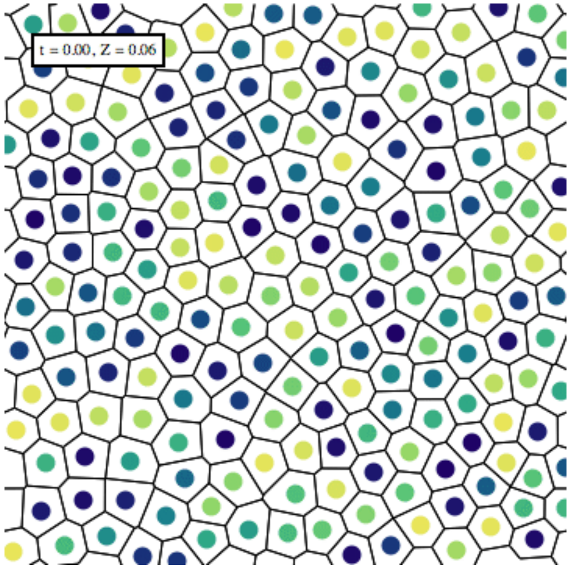
How correlated cell movement affects synchronization of coupled oscillators?

Is it better than random movement?

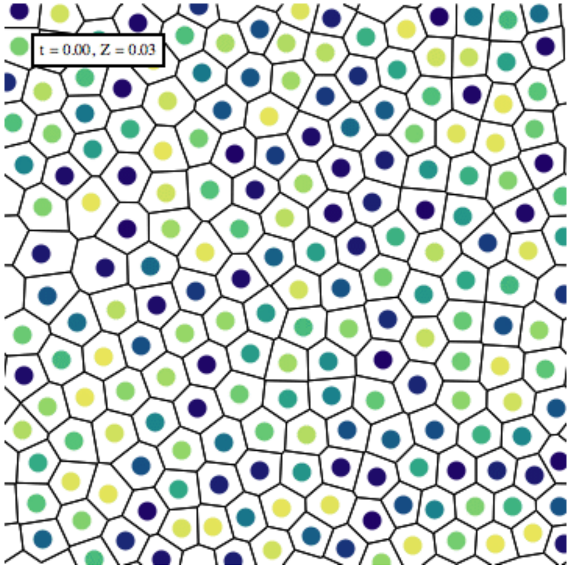
Simulations

spatial velocity correlation

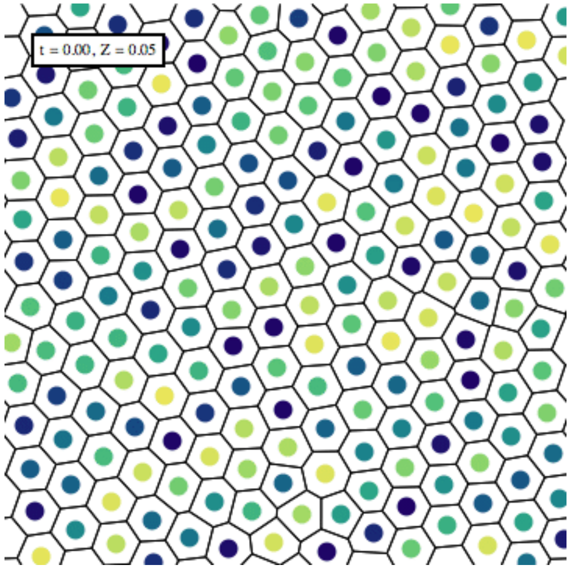
uncorrelated



short-range



long-range



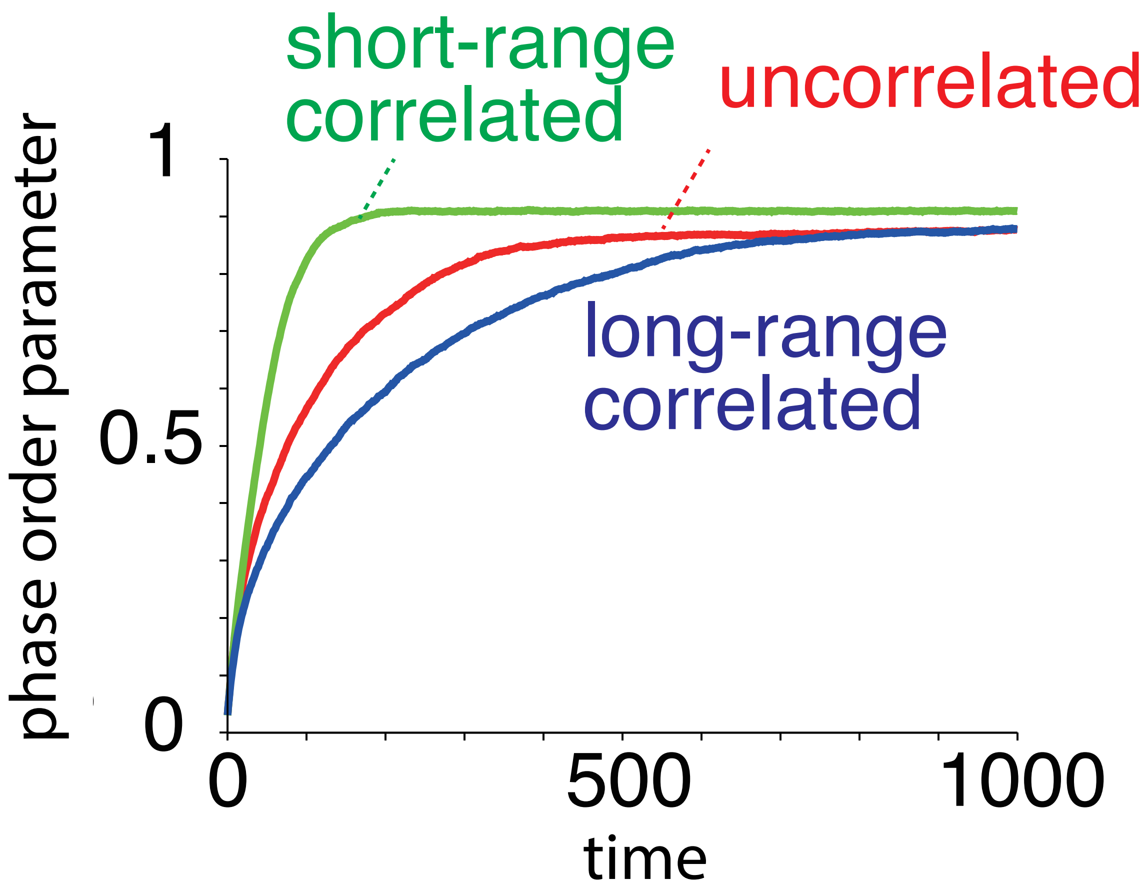
polygons : cells

color : phase of oscillation

Quickest sync. with a short-range velocity correlation

Uriu & Morelli 2014 Biophys. J

Optimal velocity correlation

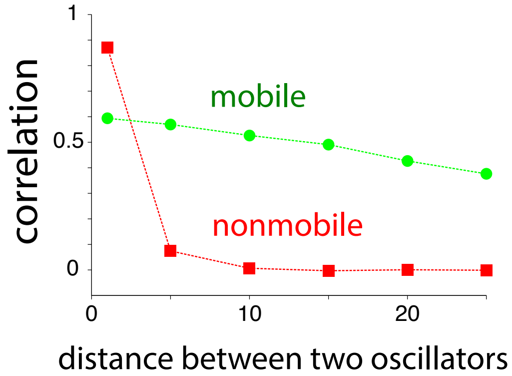


Velocity correlation length of 2~3 cell diameters is optimal for synchronization of oscillators.

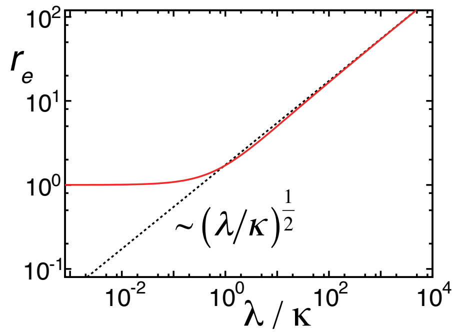
Uriu & Morelli 2014 Biophys. J

Summary

- Locally coupled oscillators can attain high local correlations, but these local correlations prevent global sync.
- Mobility of oscillators disturbs local sync., but this is good for global sync.



- Effective interaction range extends with the square root of mobility.



- A short-range velocity correlation is optimal.
- The optimal correlation length in simulations is close to the one observed in fish.