Spatial moment models for collective cell behaviour

Banff International Research Station
12-16 November 2018

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Te Pūnaha Matatini
Data ▪ Knowledge ▪ Insight

Michael Plank

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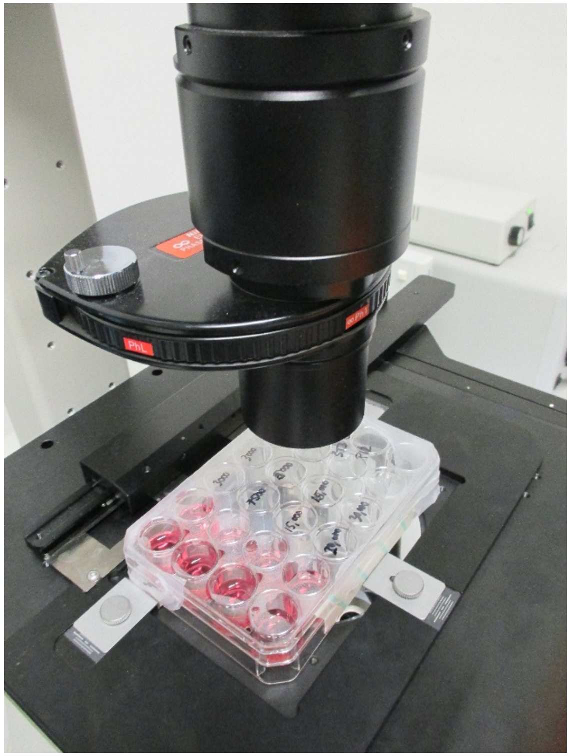
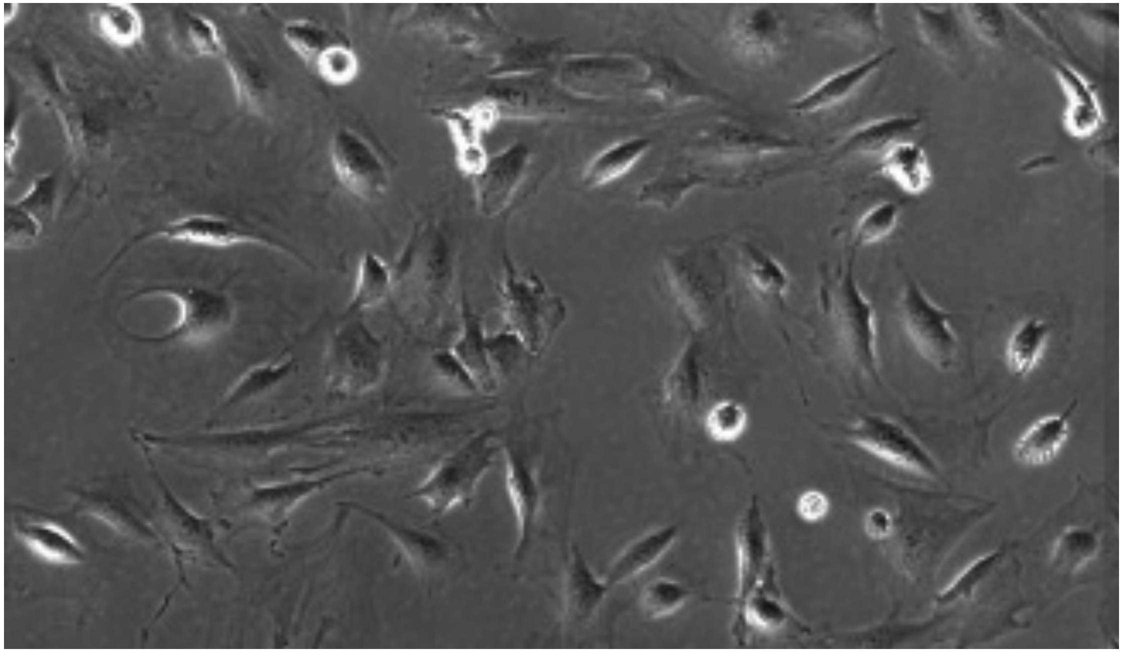
Te Pūnaha Matatini - *'the meeting place of many faces'*



- Collective cell behavior: important applications in cancer, tissue repair and embryogenesis
- Cell-cell interactions affect movement and proliferation
- This plays an important role in the collective behaviour



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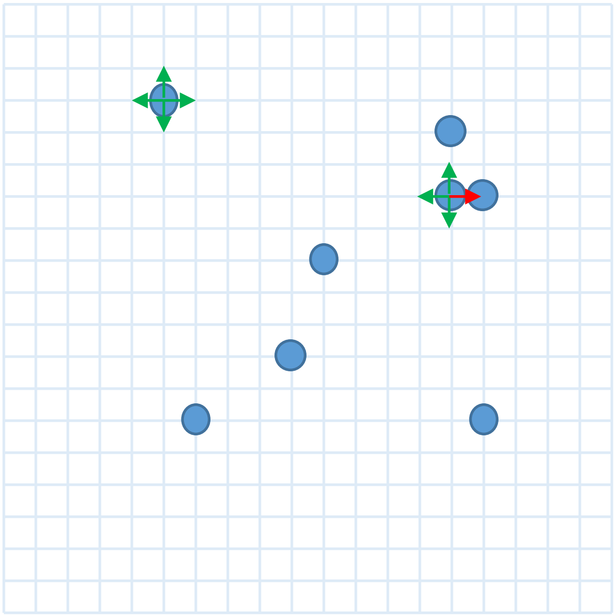
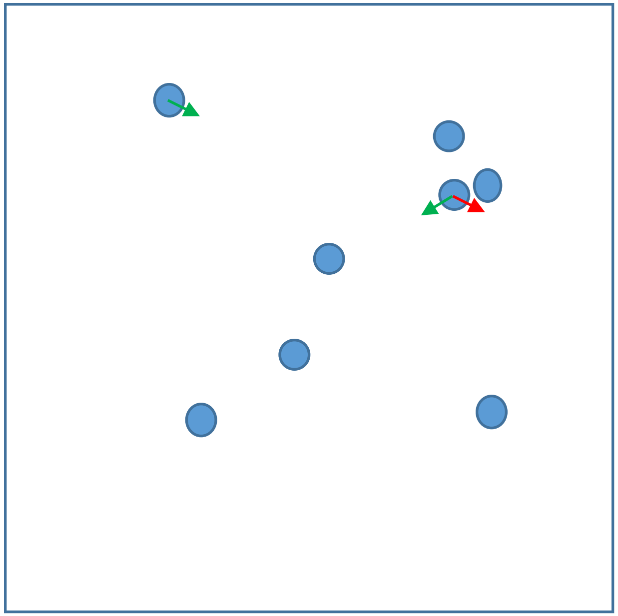
Lattice model



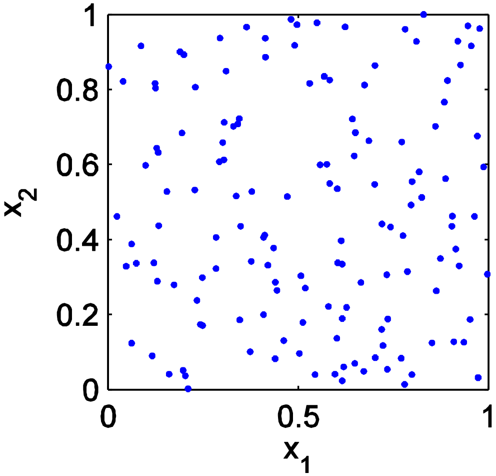
Non-lattice model



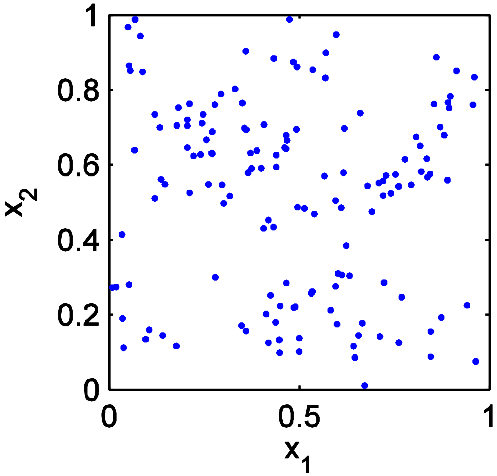
$$\frac{\partial p_{n,m}}{\partial t} = \frac{k}{4}(1 - p_{n,m})(p_{n-1,m} + p_{n+1,m} + p_{n,m-1} + p_{n,m+1})$$
$$-\frac{k}{4}p_{n,m}(4 - p_{n-1,m} - p_{n+1,m} - p_{n,m-1} - p_{n,m+1})$$

Spatial moments?

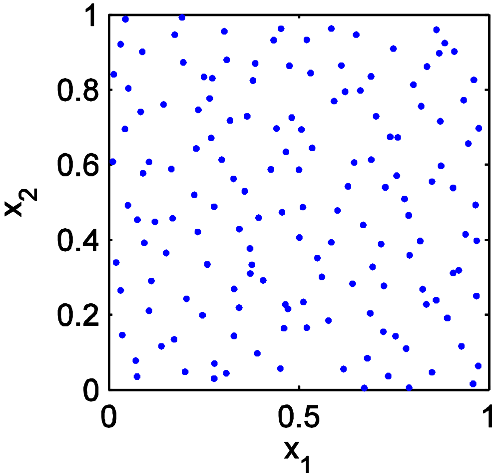
$$\frac{\partial p}{\partial t} = D\nabla^2 p$$



Poisson



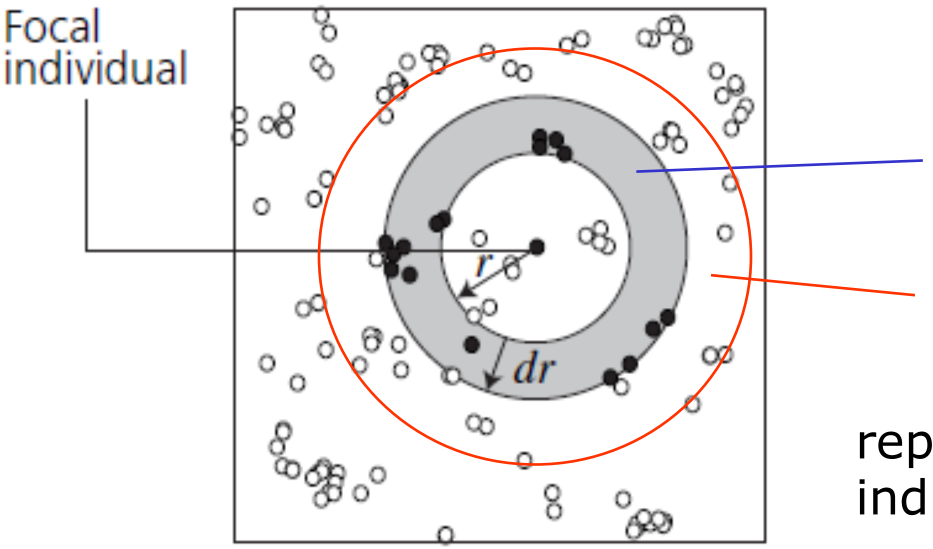
clustered



segregated

Measuring spatial structure:

pair correlation function



take one individual

count number of neighbours in a ring of radius r to r + dr.

repeat over all concentric rings

repeat for all individuals

obtain the average over individuals, dividing by square of density gives pair correlation C(r) as a function of distance r

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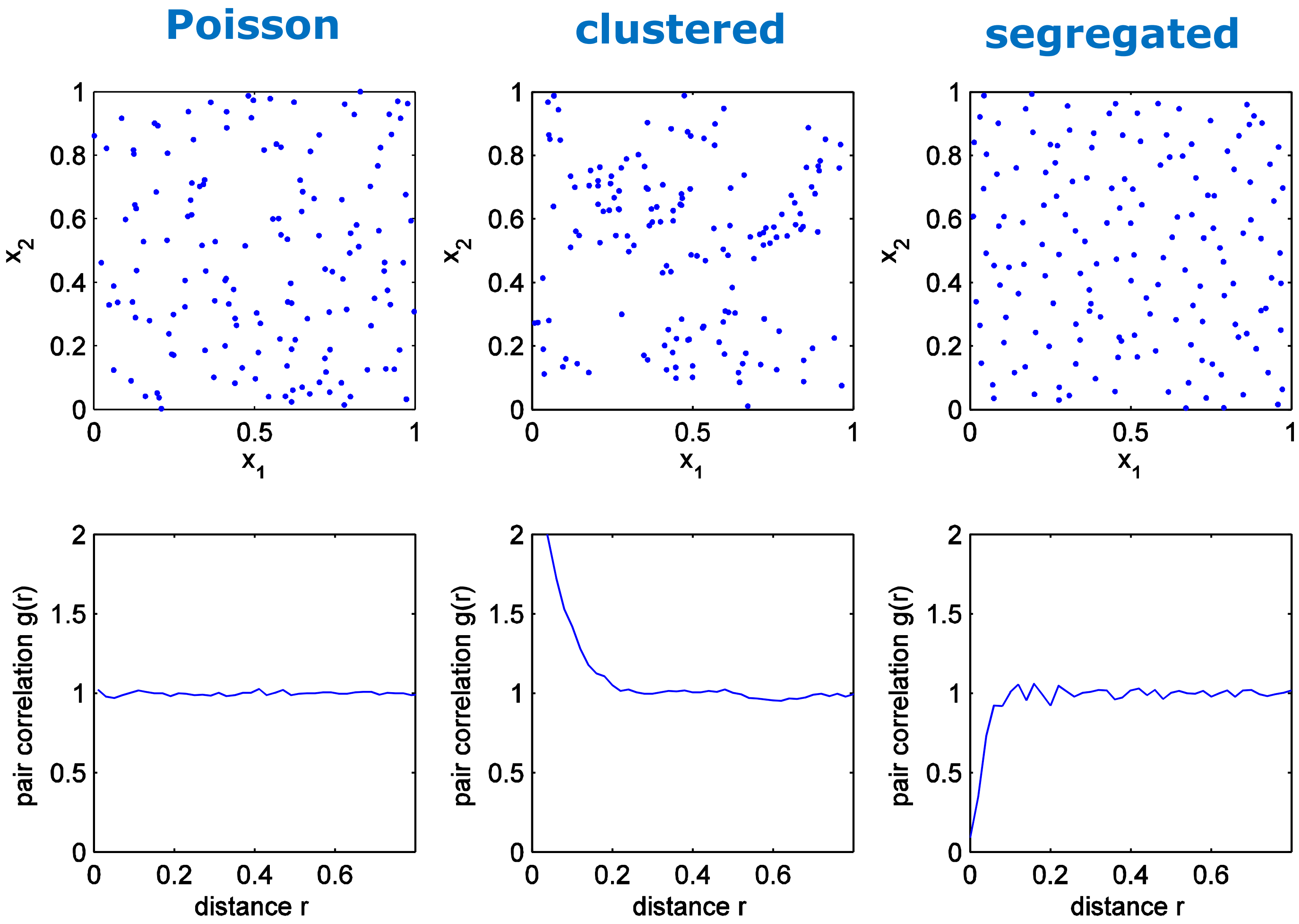

Plank and Law
(2015) BMB

- The pair correlation function contains some information about spatial structure
- “Cell’s eye view” of the population

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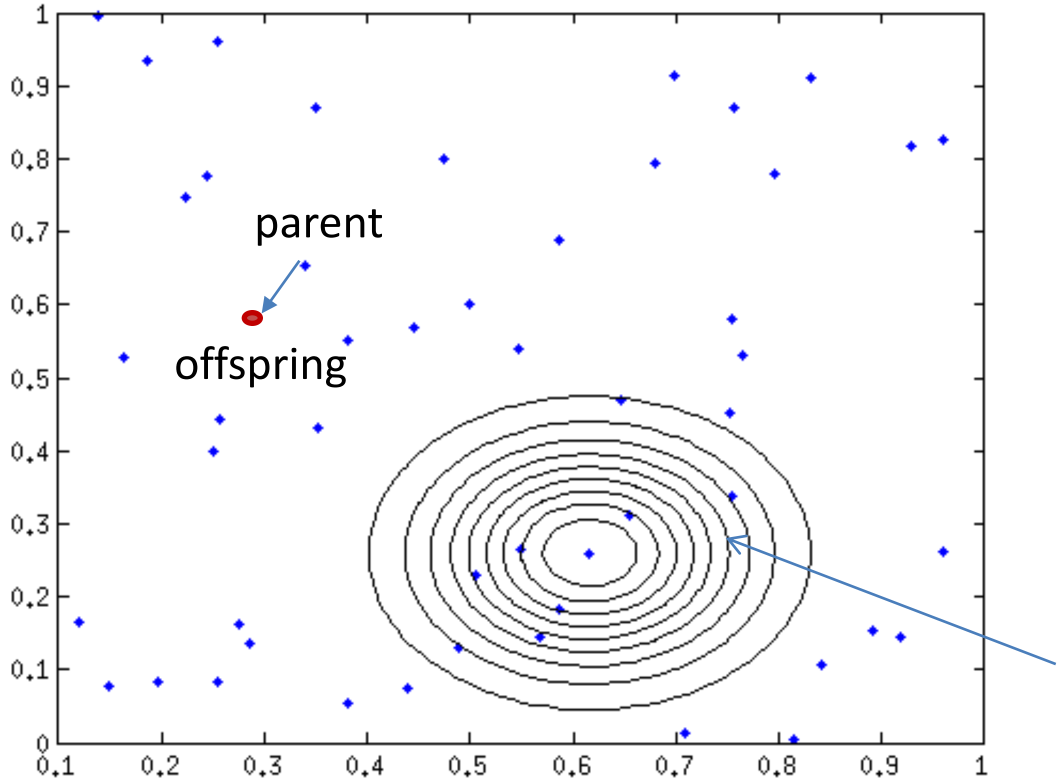
Simple example: spatial logistic model

(Bolker & Pacala 1997, Dieckmann & Law 2000)



Constant probability of reproduction

Dispersal of offspring from parent:

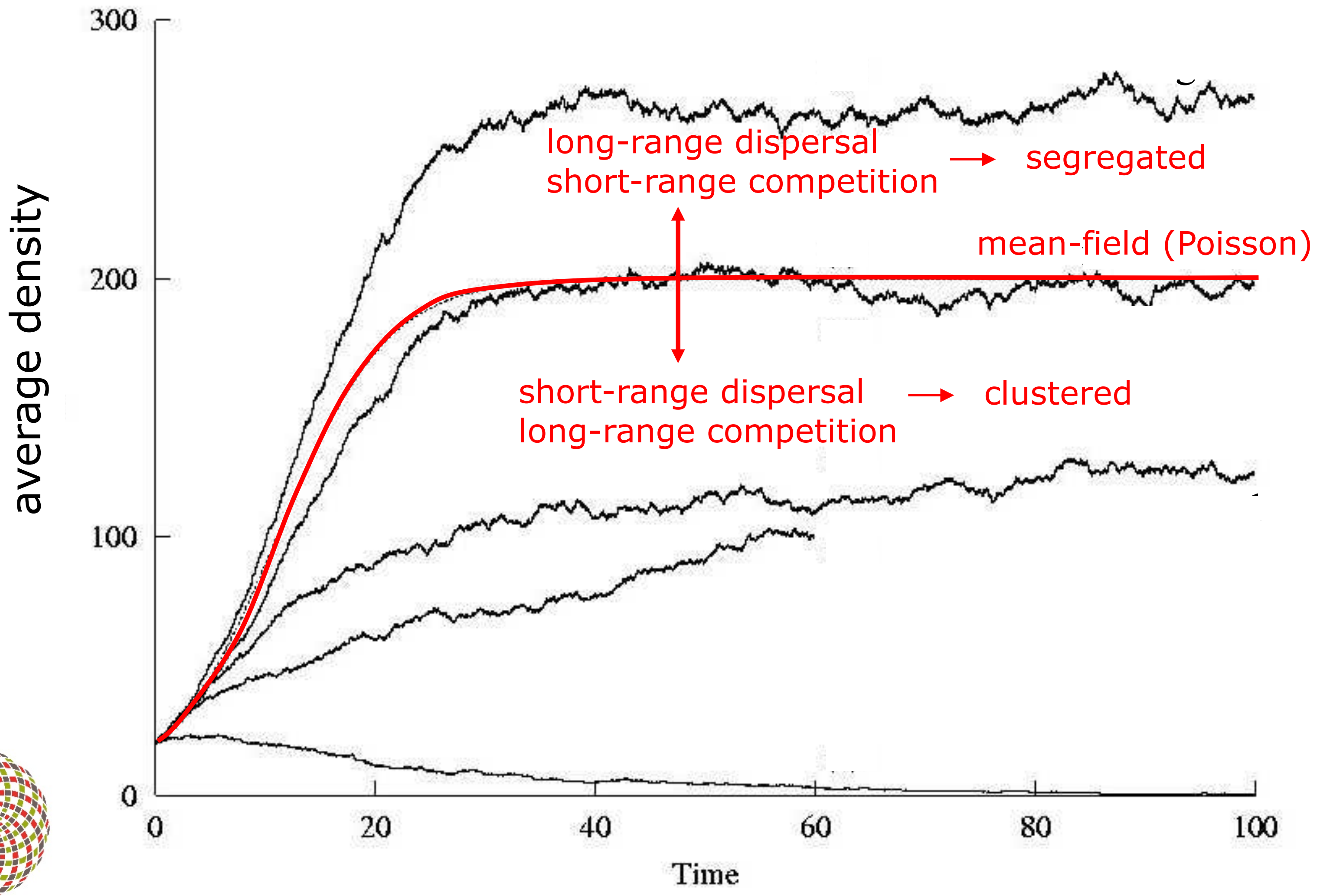
- generates **clustering**

Competition from neighbours increases death rate:

$$d_i = d_0 + d_1 \sum_{j=1}^{N} w\left(\left|x_i - x_j\right|\right)$$

- generates **segregation**

solutions of the IBM



Law, Murrell and Dieckmann Ecology 2003 84:252

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Spatial moment dynamics

First moment $N(t)$ = average density of agents

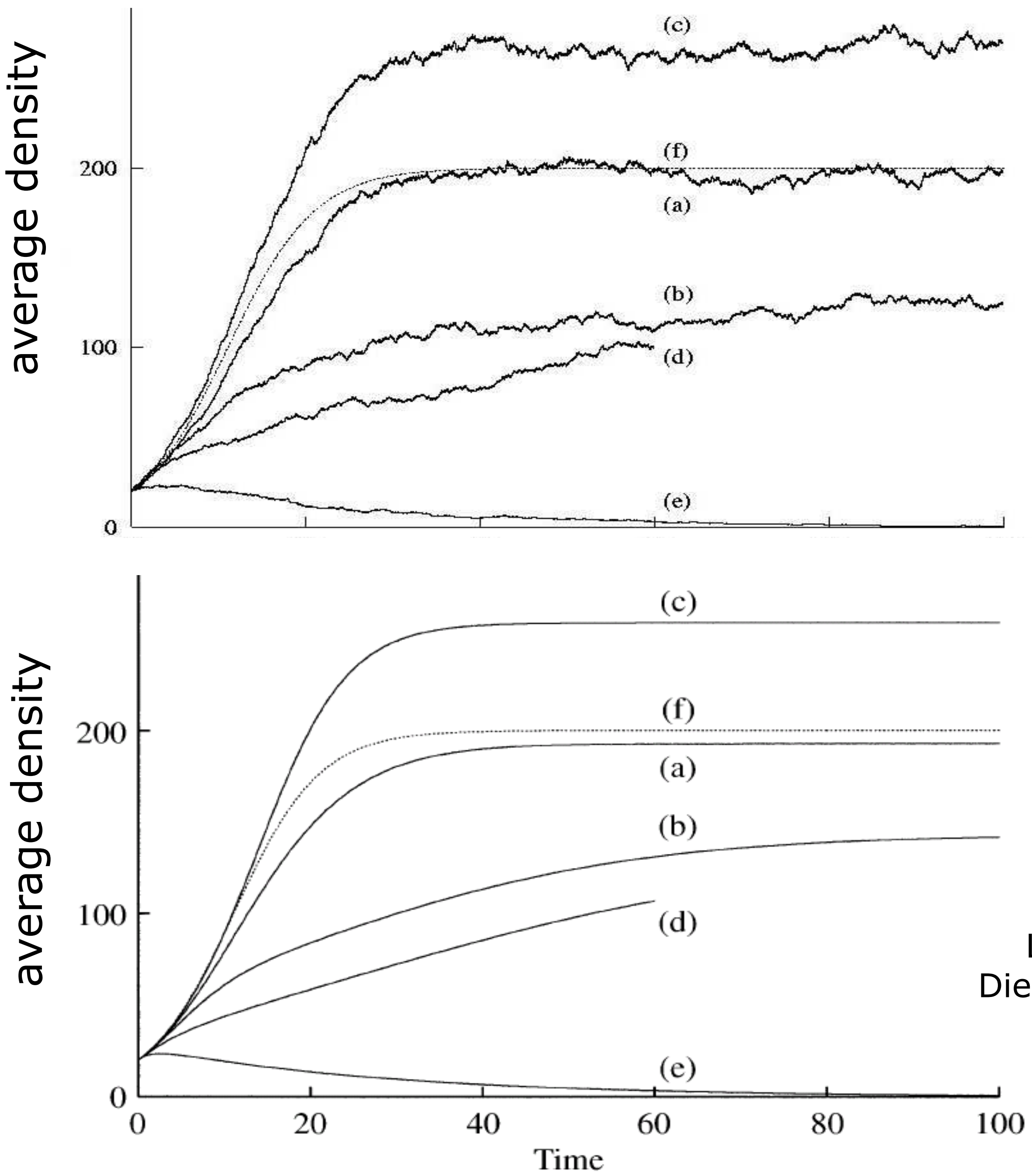
Second moment $C(\xi, t)$ = average density of pairs of agents separated by displacement ξ

$$\frac{dN}{dt} = \underset{\substack{\uparrow \\ \text{births}}}{rN} - \underbrace{d_0 N - d_1 \int w(\xi)\, C(\xi) d\xi}_{\text{deaths}}$$

$\frac{\partial C}{\partial t}$ depends on density of triplets, etc.

Need a moment closure
“Classical” (implicit) closure is $C(\xi) = N^2$, ignores structure. Dynamics reduce to logistic equation:

$$\frac{dN}{dt} = rN - d_0 N - d_1 N^2$$



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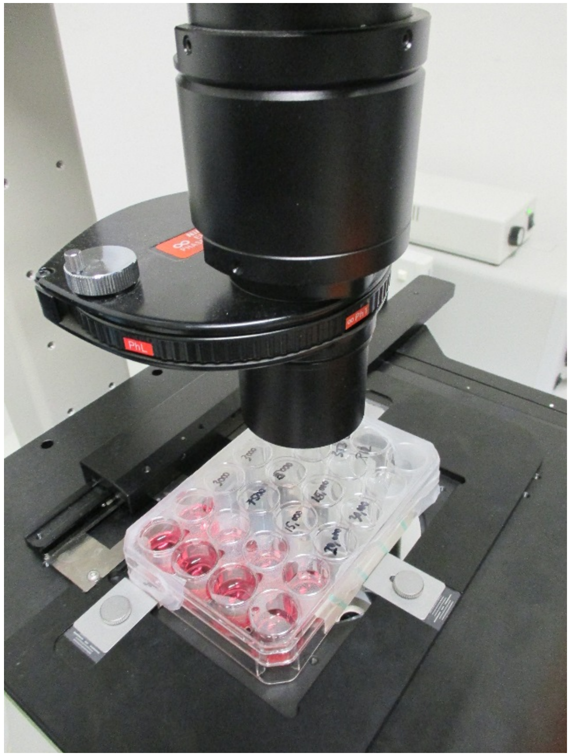
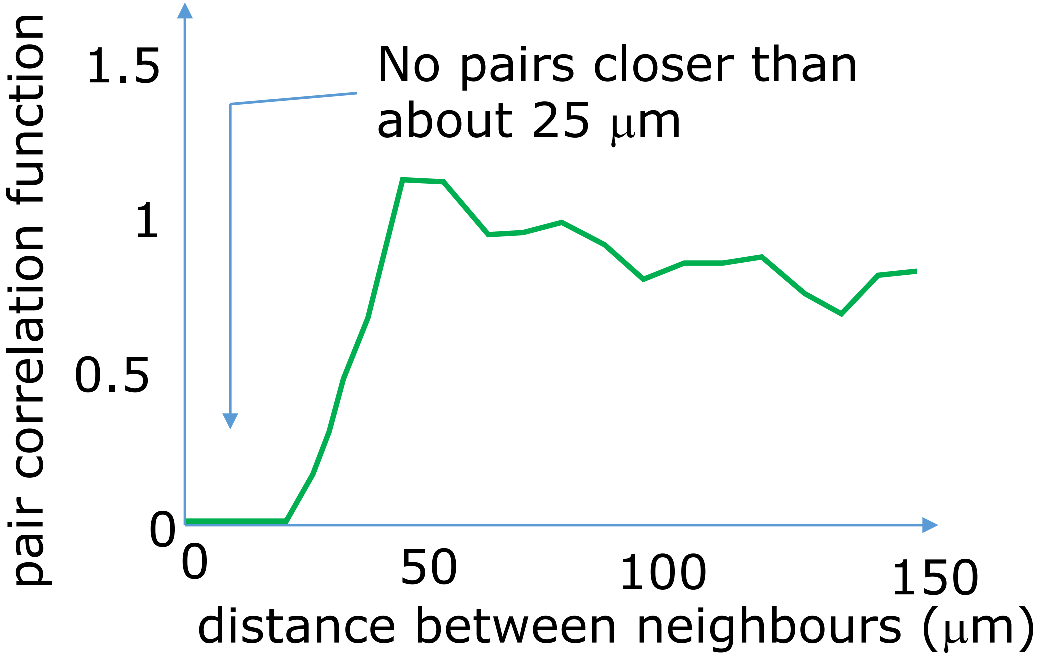
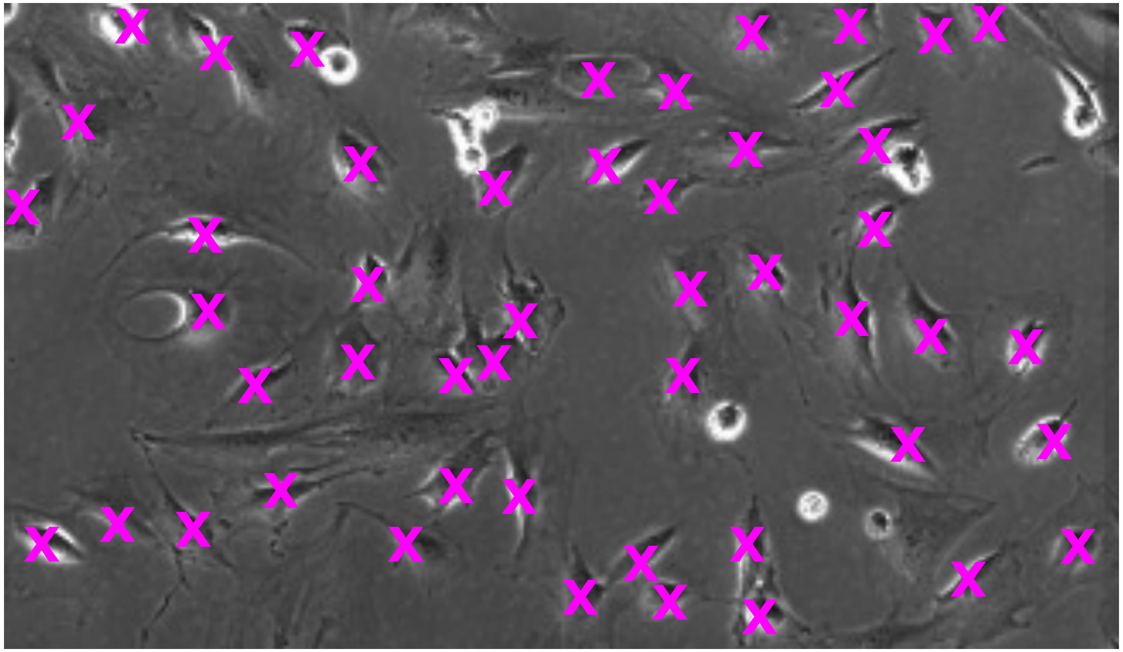




No pairs closer than about 25 μm



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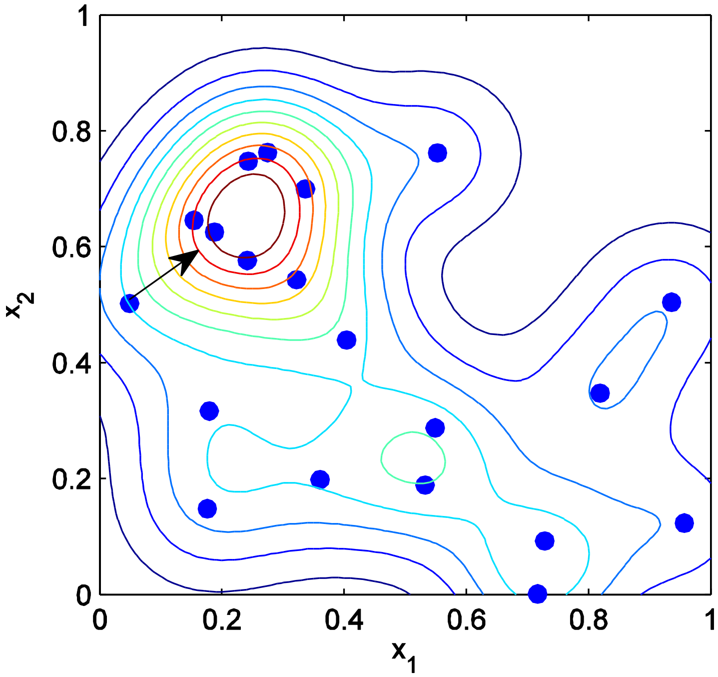
Existing models allow neighbour-dependent **movement rates**

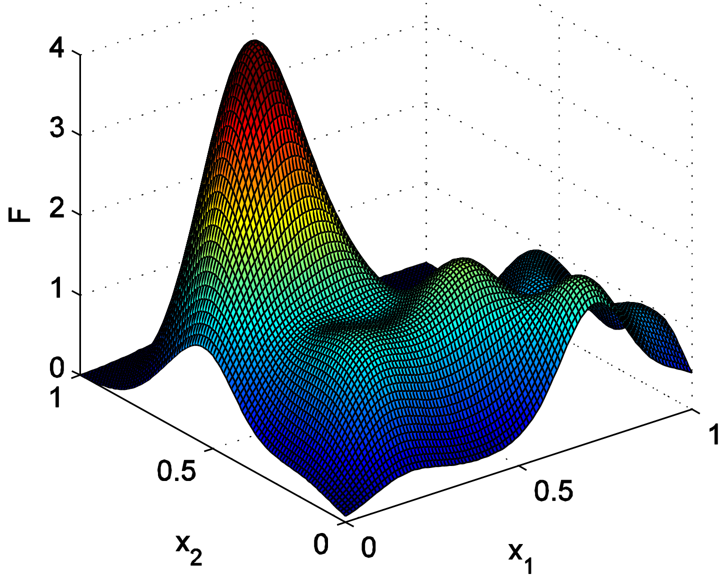
But we found this could not reproduce the sort of spatial structure seen in experimental cell populations

Instead we developed a new model for neighbor-dependent **directional bias**

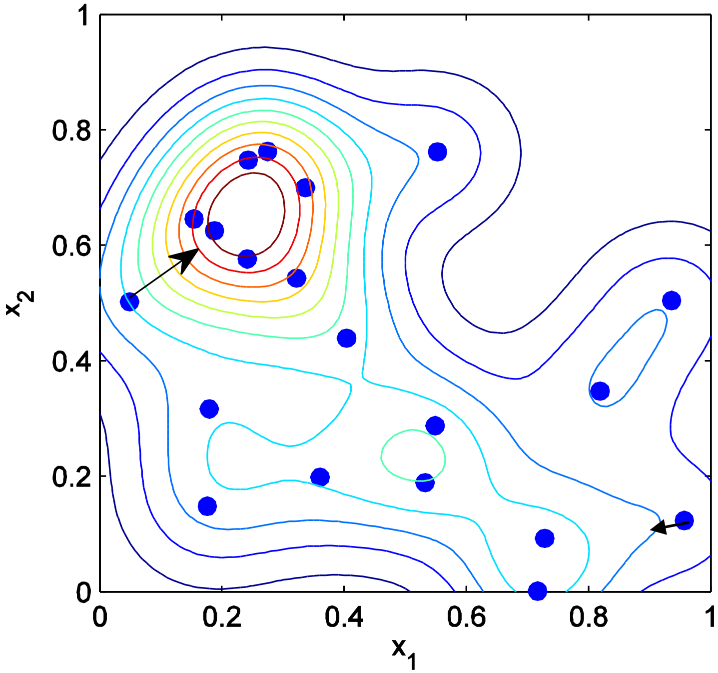


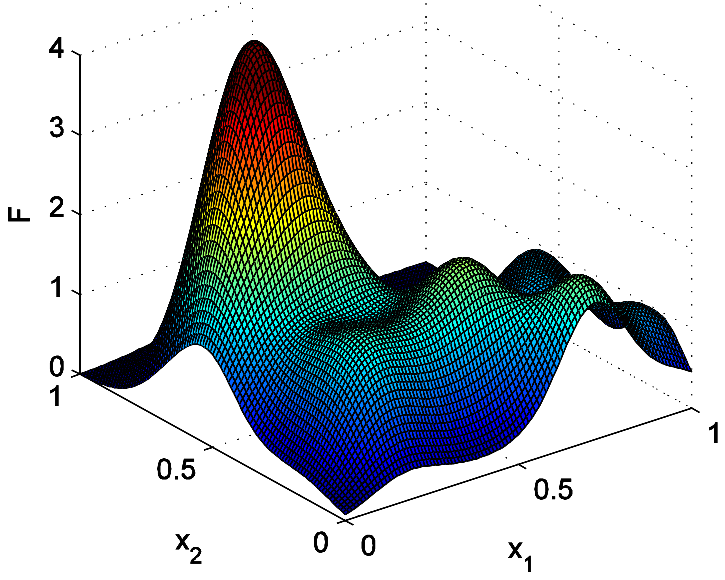
crowding surface

$$F(x) = \sum_i w(x - x_i)$$



crowding surface $F(x) = \sum_i w(x - x_i)$

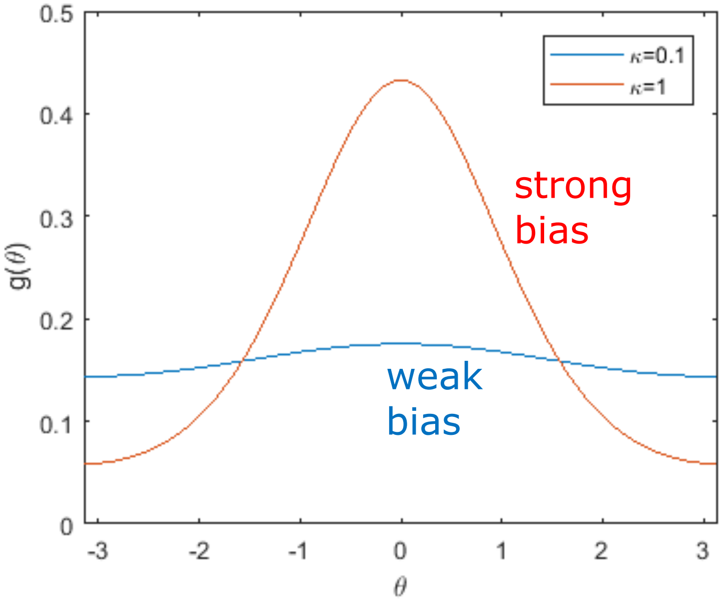




- Constant probability of movement
- Fixed distribution of step length
- Each cell biased to move in direction of $\pm\nabla F$ with bias strength $\kappa = |\nabla F|$
- Von Mises distribution of direction θ:

$$g(\theta) = Ce^{\kappa \cos(\theta - \theta_0)}$$

- Soft not hard interactions



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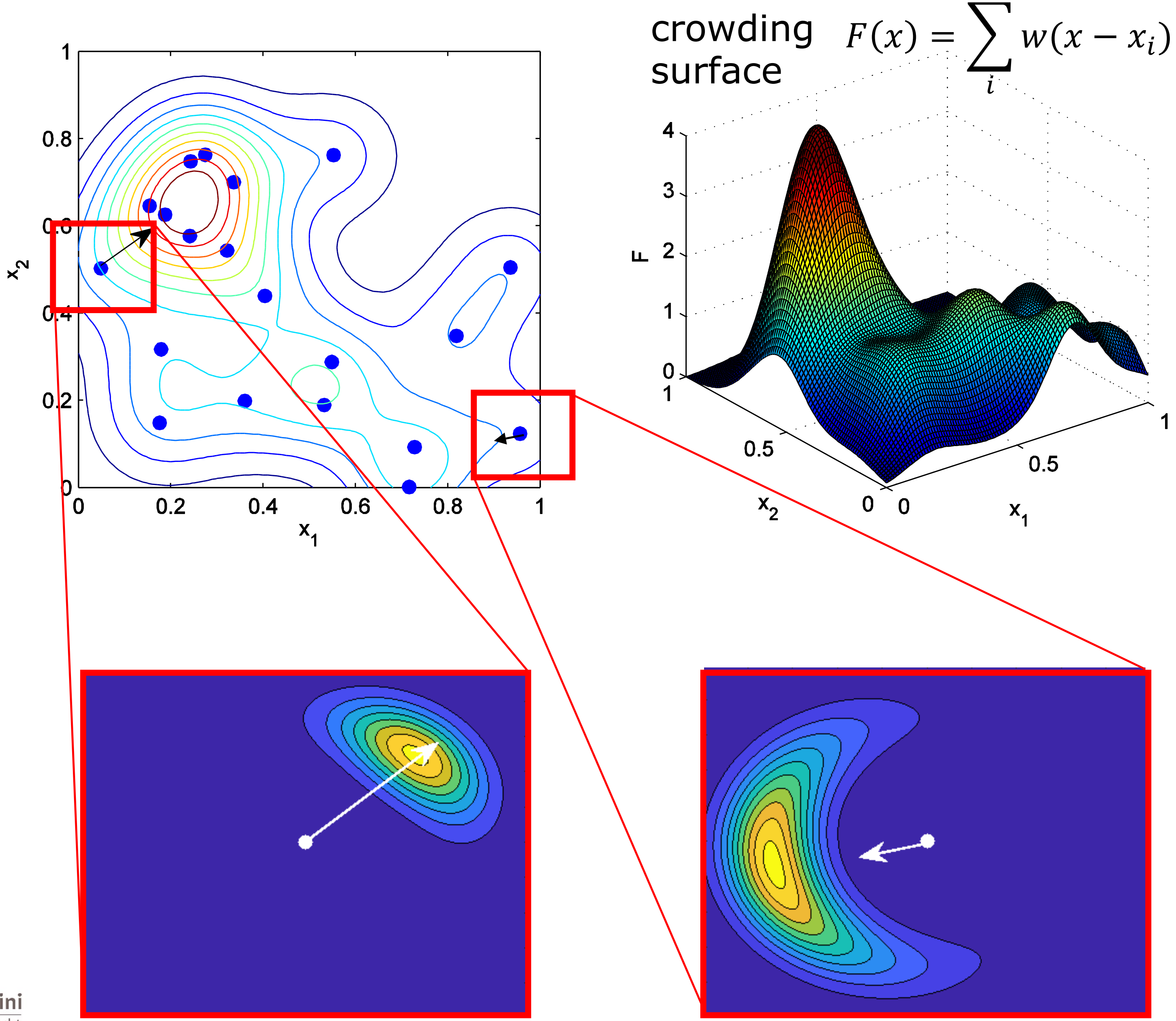
crowding
surface

$$F(x) = \sum_i w(x - x_i)$$



Spatial moment dynamics

1st moment (average density) is constant if there is no birth/death

2nd moment:

$$\frac{\partial}{dt}C(\xi,t) = -MC(\xi,t)$$

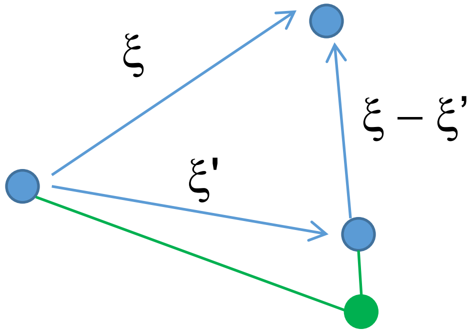
rate of change of pairs at displacement ξ

prob. there is a pair at ξ and one of the agents moves

prob. there is a pair at ξ′

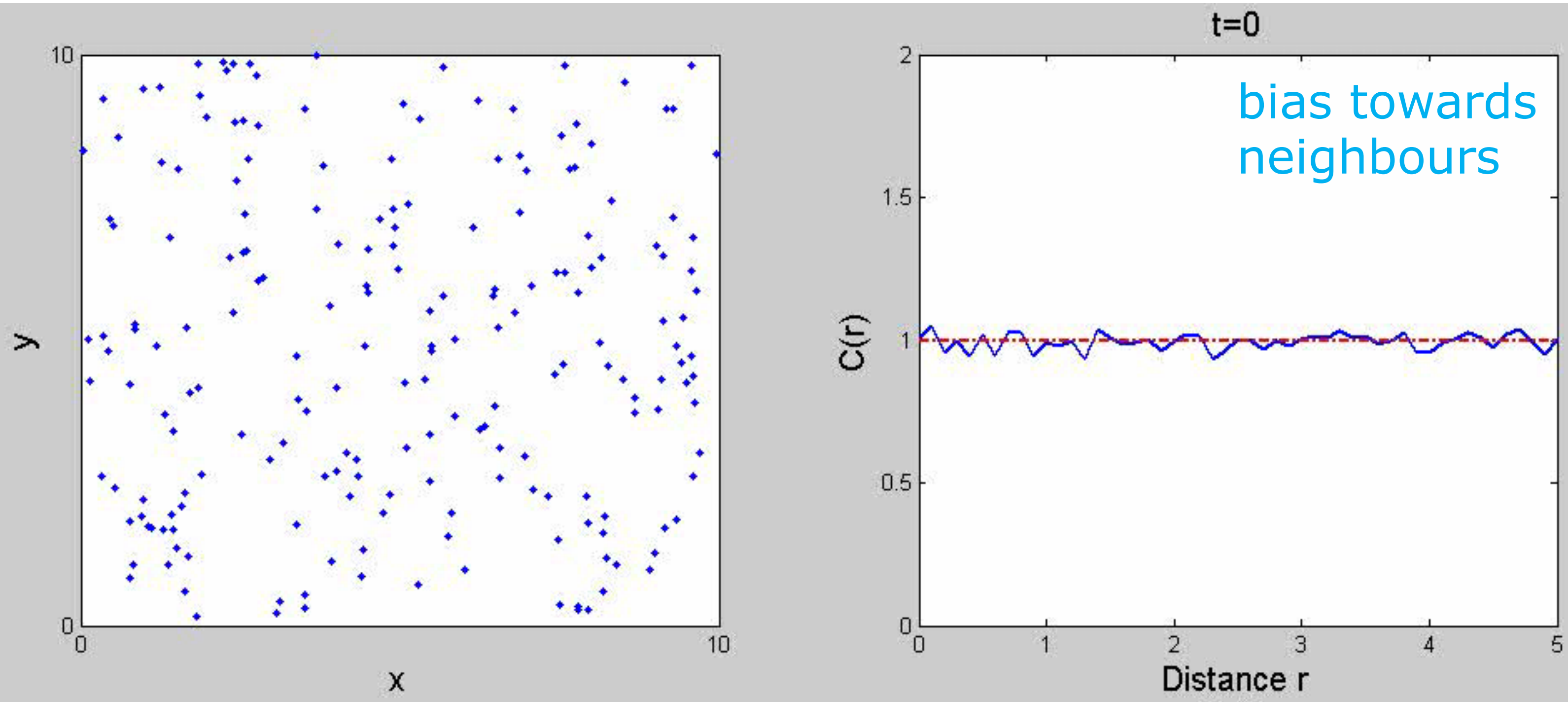
prob. agent moves to make the pair at ξ

depends on triples T via bias mechanism

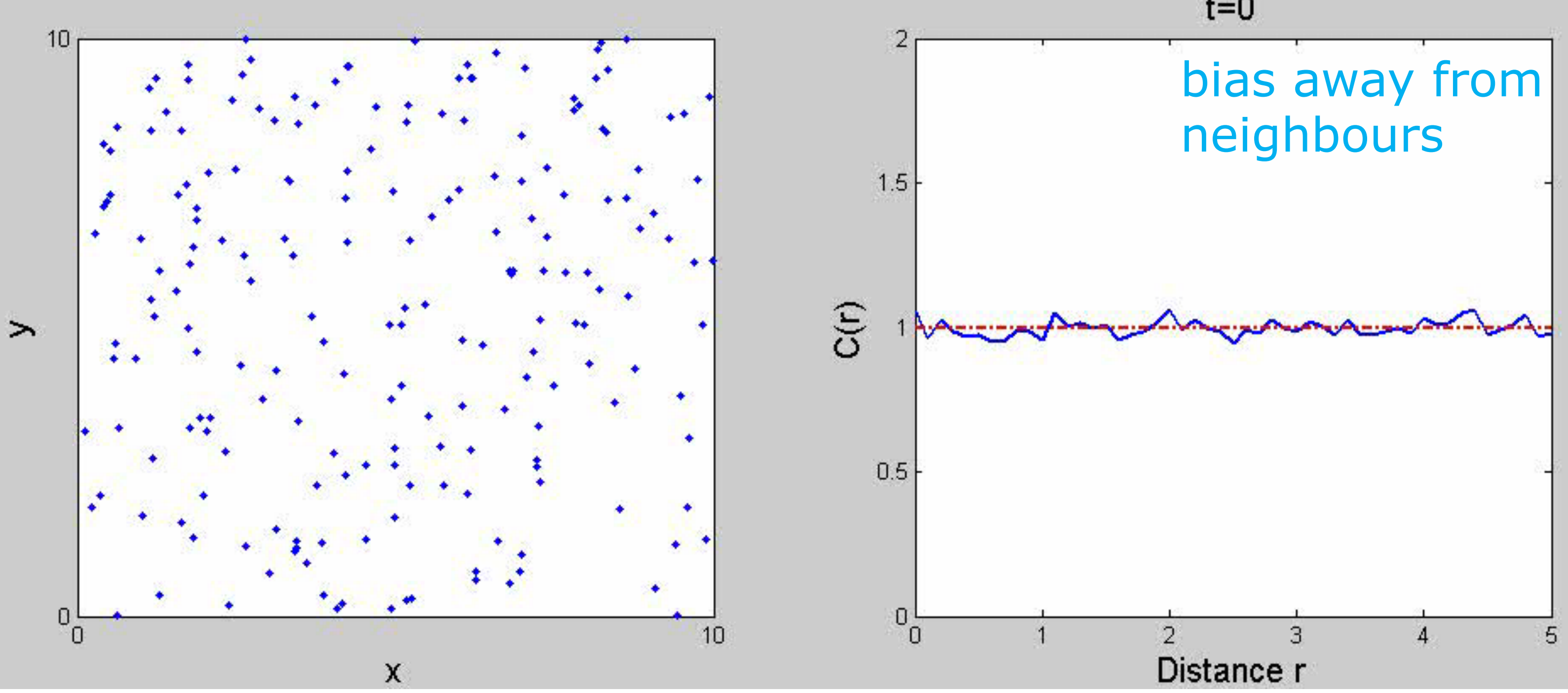


$$b(\xi) = \int \nabla w(\xi')\frac{T(\xi,\xi')}{C(\xi)}d\xi' + \nabla w(\xi)$$

Binny et al (2015)
Interface

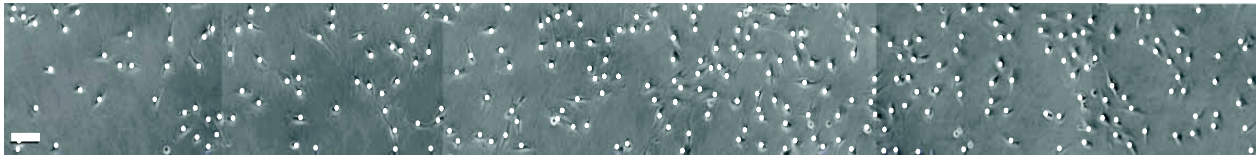


bias towards neighbours

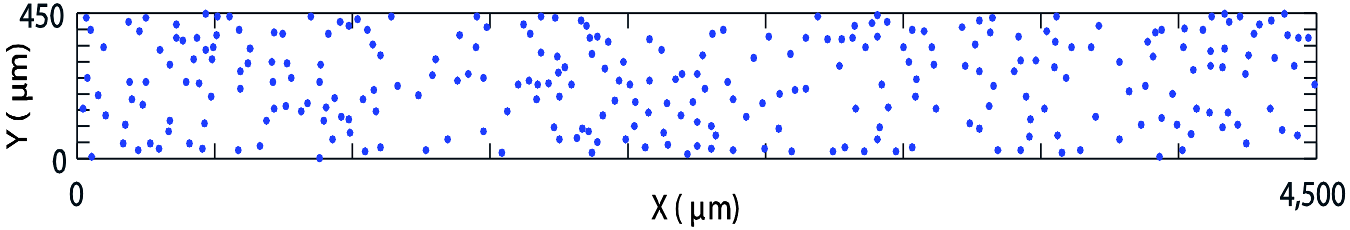


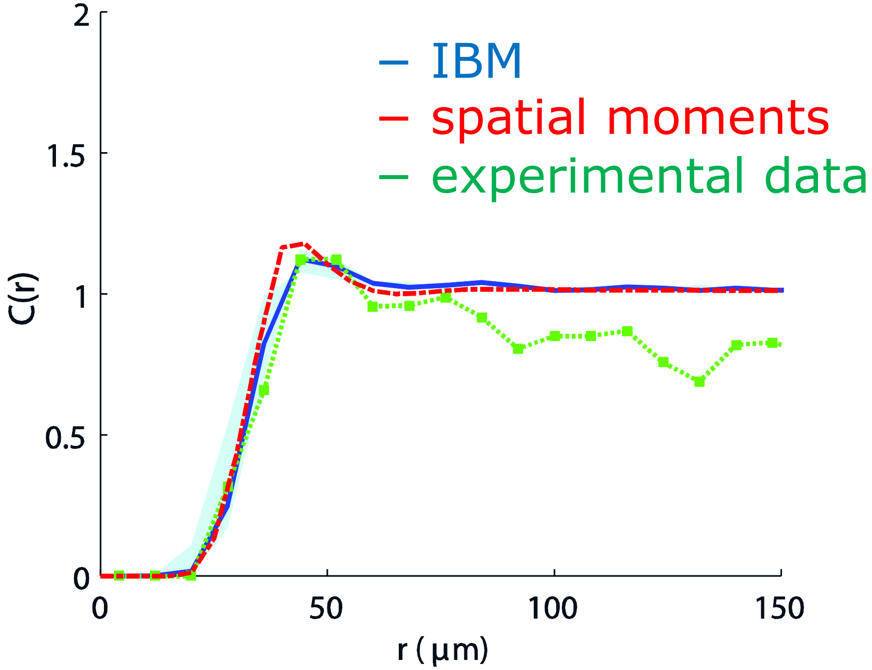
bias away from neighbours

Can model reproduce spatial patterns seen in experiments?



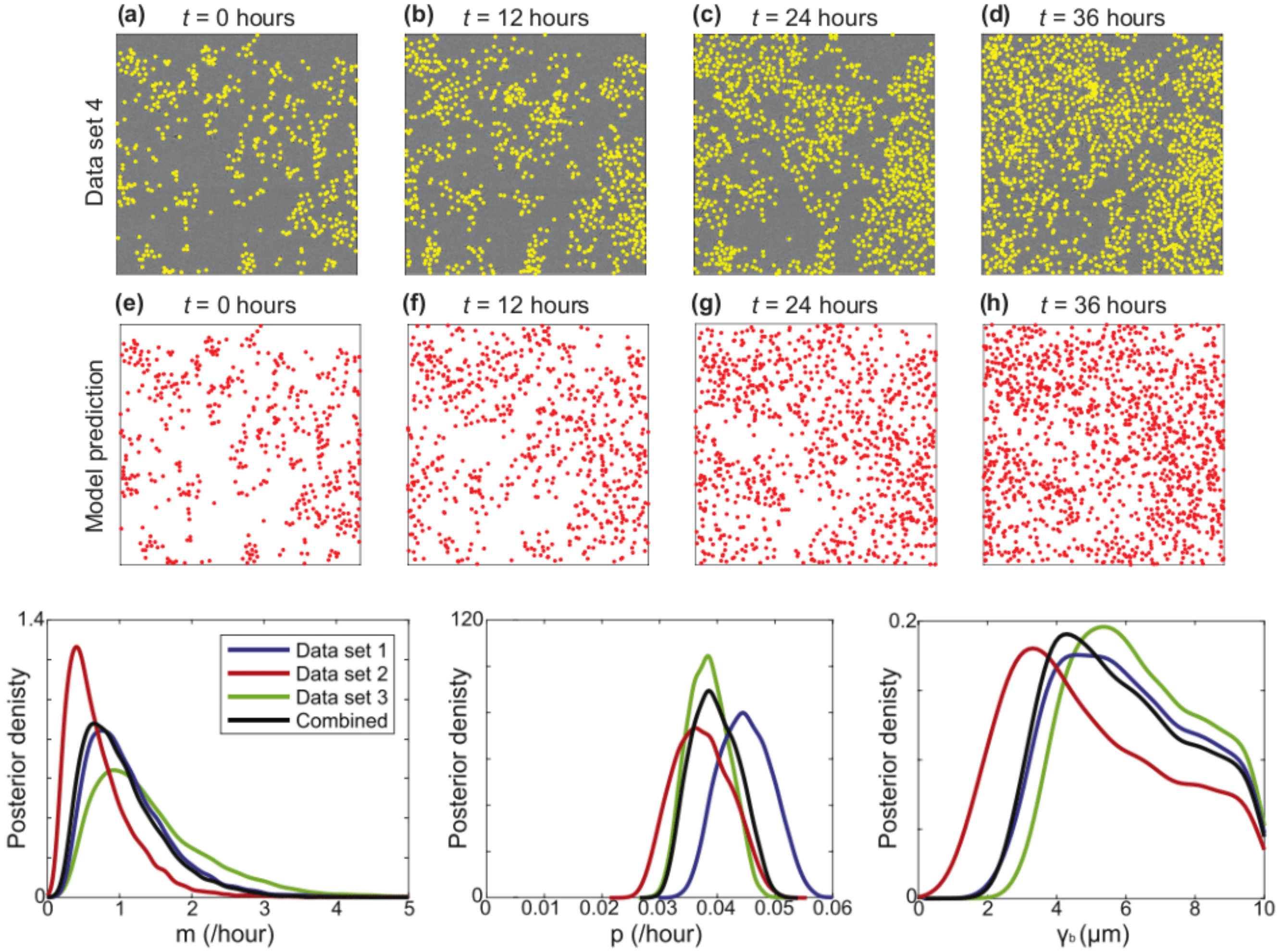
Cells biased to move **away** from neighbours as a result of physical contact





Binny et al (2015)
PeerJ

Parameter estimation via ABC



Browning et al (2017) JTB

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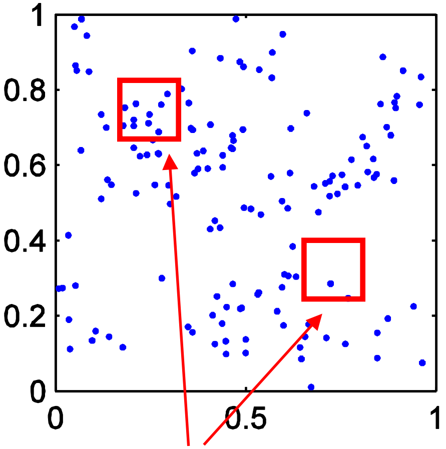
Summary

- **Spatial structure** is important in many situations where individuals interact with one another over defined spatial scales
- Examples include community ecology, epidemiology and collective cell behavior
- We have developed a new model that allows **neighbour-dependent bias**
- This is one way of capturing the spatial structure seen in experimental cell populations

Spatially heterogeneous populations

Spatially homogeneous

$$\frac{dN}{dt} = \overset{\text{birth}}{\overset{\downarrow}{rN}} - \overset{\text{neighbour-independent death}}{\overset{\downarrow}{d_0 N}} - \overbrace{d_1 \int w(\xi)\, C(\xi) d\xi}^{\text{neighbour-dependent death}}$$



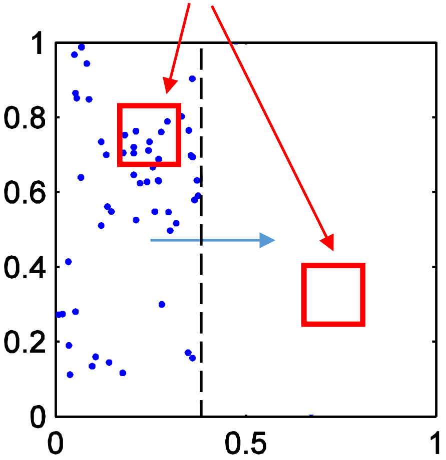
different windows have same statistics

Spatially heterogeneous

$$\frac{\partial}{\partial t} N(x) = \overbrace{r \int k(\xi) N(x-\xi) d\xi}^{\text{birth}} - \overset{\text{neighbour-independent death}}{\overset{\downarrow}{d_0 N(x)}}$$

$$\underbrace{-d_1 \int w(\xi)\, C(x, x+\xi) d\xi}_{\text{neighbour-dependent death}}$$

different windows have different statistics



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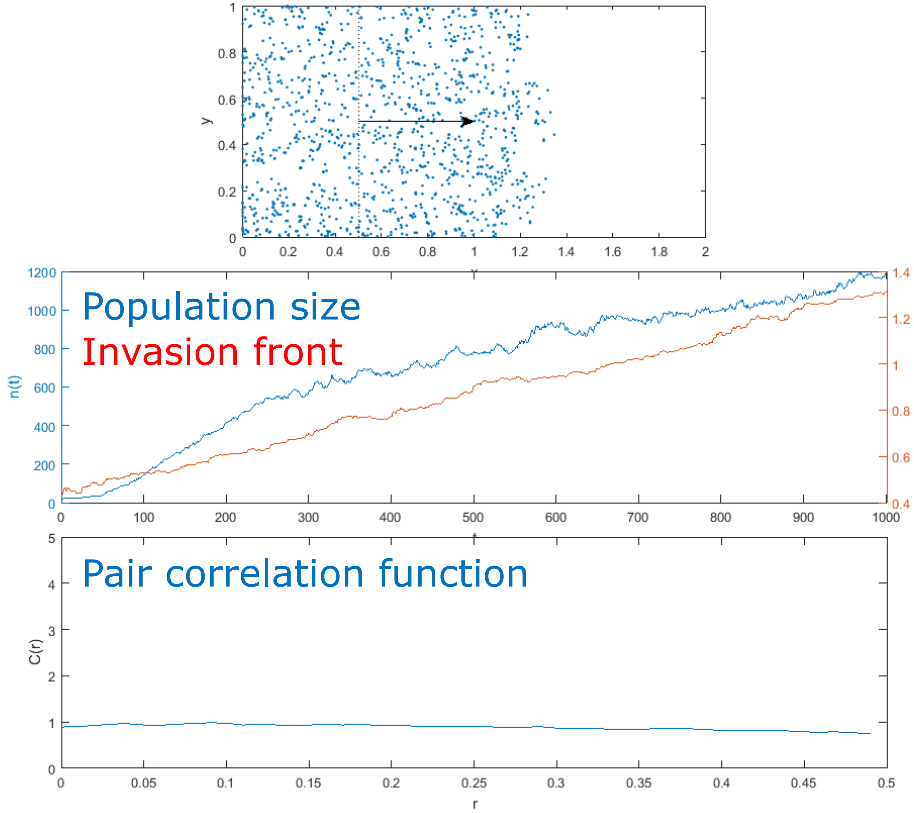
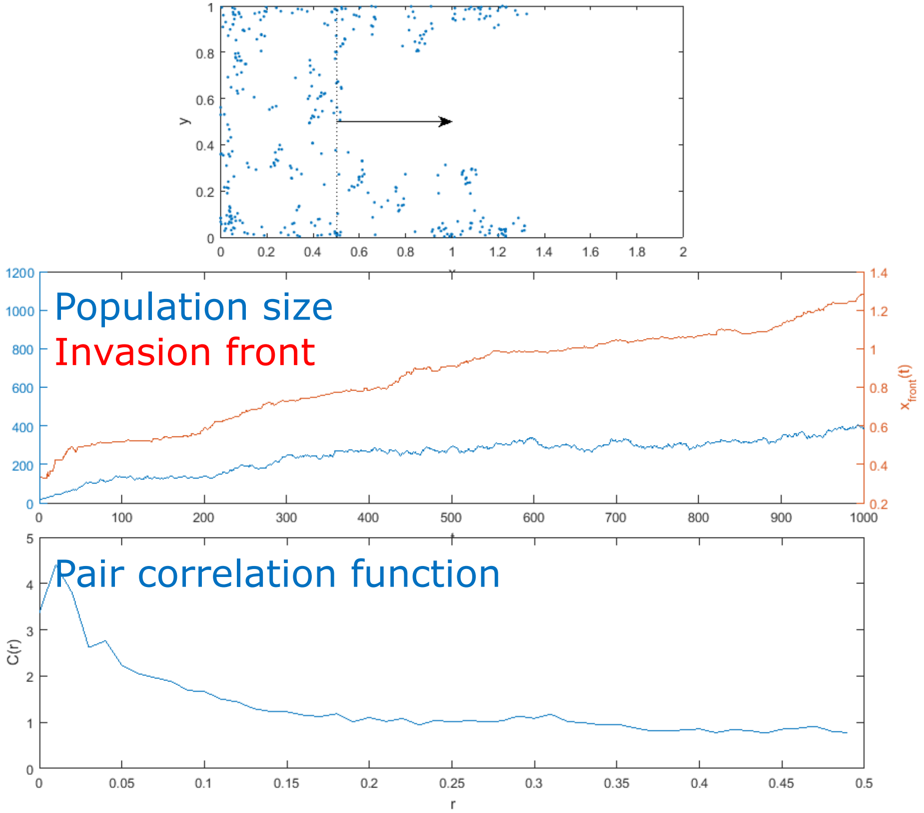
Spatially heterogeneous populations

Strong short-range competition



Weak long-range competition



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Thank you!

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- Rachelle Binny, UC
- Alex James, UC
- Richard Law, University of York
- Parvathi Haridas, QUT
- Matthew Simpson, QUT
- Alex Browning, QUT

References

- Binny RN., Plank MJ. and James A. (2015) Spatial moment dynamics for collective cell movement incorporating a neighbour-dependent directional bias. Interface 12(106) 20150228
- Binny RN., Haridas P., James A., Law R., Simpson MJ. and Plank MJ. (2016) Spatial structure arising from neighbour-dependent bias in collective cell movement. PeerJ 4(16) e1689
- Bolker B, Pacala SW (1997) Using moment equations to understand stochastically driven spatial pattern formation in ecological systems. Theor Popul Biol 52(3):179–197
- Browning A, McCue SW, Binny RN, Plank MJ, Shahe ET, Simpson MJ (2017) Inferring parameters for a lattice-free model of cell migration and proliferation using experimental data. Journal of Theoretical Biology, in press.
- Dieckmann U, Law R (2000) Relaxation projections and the method of moments. In: Dieckmann U, Law R, Metz JAJ (eds) The Geometry of ecological interactions: simplifying spatial complexity. Cambridge University Press, Cambridge, pp 412–455
- Law R, Murrell DJ, Dieckmann U (2003) Population growth in space and time: spatial logistic equations. Ecology 84(1):252–262
- Plank MJ. and Law R. (2015) Spatial Point Processes and Moment Dynamics in the Life Sciences: A Parsimonious Derivation and Some Extensions. Bulletin of Mathematical Biology 77(4): 586-613.