Bringing shape into development (1)
Root of Arabidopsis
LAST TIME:

Classical models in development: Pattern formation: NO CELLS!
• Turing patterns (domain dependence, new stripes when growing)
• positional information: imposed gradient
  (interactions make much of the pattern)
• clock wavefront: oscillation → spatial pattern, growing domain
  indeed “generic”? , neutral drift, also many morphological differences

NEXT

Cell-based models of development:

Salazar-Ciudad:
morphostatic development: autonomous and induction
morphodynamic: (collective) cell movement (changes of NB.)
How to cope with complexity of biological systems?

earlier:

simplify: use known mechanism as search image (excitable media/ turing patterns)

alleviate parameter curse by adding evolution (Lac operon)

exploit constraints - shortcut by optimization (FBA)

TODAY:

Simplify dynamics, but use complex use structure
Towards multilevel modeling of development

- feedback of shape/size on low level dynamics
- precise localization / emergence of sharp boundaries
- data intensive modeling in various guises
  - model fitting vs parameter fitting
- more structure less parameters

Structural information much easier to obtain than parameters!
  Often parameters have only meaning in model
  (cf parameters of gap gene network, “effective diffusion coeff”)

Positional information revisited
Example of morphogen gradient:
auxin concentration in plant roots
(also gradient of transcription factors PLT)

Grieneisen et al 2012 “morphogengineering roots” BMC sys bio
Can auxin gradient be caused by source-decay or directional transport mechanism?

scaling and positional information

default par: halflife auxin 8 days, Diff constant 600µ
scaling and positional information Source/decay mechanism

informative length should match tissue size (in root 500 µ)

characteristic length ( variation =37%);

\[ \lambda = \sqrt{\left( \frac{D}{d} \right)} \]

for default parameters: 2.4 cm!

changing decay d : low maximum (250 fold decrease)

change Doffusion D : slow dynamics:8µ/hr instead of 1cm/hr)

communication range characteristic length

(in root over whole plant)
Question: how does the plant manage to keep up gradient, and maximum given high diffusion and long lifetime of auxin?

use structural information in dynamical model

Cells, layout of cells,
localization of PIN’s (transport auxin out of cell)

Grieneisen, Xu, Marée, Hogeweg & Scheres Nature 2007
much structure, few parameters
diffusion + transport

<table>
<thead>
<tr>
<th>symbol</th>
<th>description</th>
<th>unit</th>
<th>value</th>
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<tbody>
<tr>
<td>$\Delta t$</td>
<td>time step</td>
<td>s (seconds)</td>
<td>0.1</td>
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<tr>
<td>$\Delta x$</td>
<td>space step</td>
<td>$\mu$m (microns)</td>
<td>2</td>
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<tr>
<td>$D$</td>
<td>auxin diffusion constant</td>
<td>$\mu$m$^2$/s</td>
<td>600</td>
</tr>
<tr>
<td>$P_i$</td>
<td>influx auxin permeability</td>
<td>$\mu$m/s</td>
<td>20</td>
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<tr>
<td>$P_{\text{bg}}$</td>
<td>background PIN efflux permeability</td>
<td>$\mu$m/s</td>
<td>1</td>
</tr>
<tr>
<td>$P_{\text{pin}}$</td>
<td>permeability due to basally expressed PINs, apically expressed PINs, PINs in root cap and lateral PINs of border cells.</td>
<td>$\mu$m/s</td>
<td>20</td>
</tr>
</tbody>
</table>
reflux pattern establishes auxin maximum + gradient
auxin capacitor
temporal dynamics of gradient formation by reflux loop compared to other mechanisms
auxin maximum + gradient
independent of localized production
also submersion in auxin, global auxin production
reestablishment of maximum after (laser) ablation of QC
mutants: PIN347 triple knockouts

less pins in columnella (.1) (cf f)
vascular (.35) (cf g)
border cells (.25) (cf h)
Parameter sensitivity: lateral PIN’s!

overall permeability 1000 fold
ratio lateral vs up/down 8 fold

similar for 1000 fold diffusion

( Note: observation of lateral pins!)
lateral PIN's

Profiles of roots with and without epidermal lateral PINs:

- **with epi. lat. PINs, case (a)**
- **without epi. lat. PINs, case (b)**
conclusions

SOFAR:

- Given PIN localization in STATIC cell/tissue structure
  study auxin dynamics in wildtype and mutants, exp. manipulation

  -- >

- Auxin 'capacitor'
- very fast (re)establishment of max.
- close correspondence with experiments
- quasi-equilibrium.

NEXT: study tissue dynamics at longer timescales
auxin quasi-equilibrium:
profile remains similar but higher and extended
couple cell growth and division to auxin gradient
use CPM formalism for cell growth

Auxin-regulated growth

Cytokinesis

$C > C_{\text{min}}$

Variable cycle of fast expansion

Fixed cycle of slow growth
Long term consequences
quasi-equilibrium

- slow growth of meristeme
  weeks! cell size
  # cell divisions

- after root cut:
  slow shrinking of meristeme

- Sharp meristeme zone
  emergent prop from
  continuous gradient

Very fast establishment... Long term development
Summary

seconds to weeks!

PINs $\rightarrow$ 'reversed fountain' $\rightarrow$ auxin peak at QC $\rightarrow$ sharp meristem zone

Very fast establishment... Long term development
The role of cell + tissue shape(!)

Grieneisen, thesis 2009

see also
Thea van der Berg,.. Kirsten ten Tusscher 2016, Development: Modeling halotropism: a key role for root tip architecture and reflux loop remodeling in redistributing auxin
conclusions

- Auxin reflux mechanism very efficient
- One mechanism explains dynamics from seconds to days
- Large scale information integration
- Robustness to parameter changes
- Sensitivity to (some) structural changes
  - Lateral pins; cell/tissue shape
- Emergent sharp boundaries / cell types
- Potential sensitivity to external conditions
- Data intensive modeling (mutants) but NOT parameter fitting
- Classical mechanism for positional information
  - “Too small or too slow”