Recursive Algebraic Modelling of Gene Signalling, Communication and Switching **(Pea Leaf and Arabidopsis Trichomes)**

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and

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Algebraic Biology
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Philosophy and Rationale

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"One of the principal objectives of theoretical research in any department of knowledge is to find the point of view from which the subject appears in its greatest simplicity."

J. Willard Gibbs

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- Complex computer programs (GPS) are organized sets of JUST simple instructions.

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Non-matching scales between model and reality - macroscopic (pde) models of cellular processes.

The Pea Leaf

Senior Study Vegetables, Purdue University

Young's 1983 Model of Pea Leaf Development

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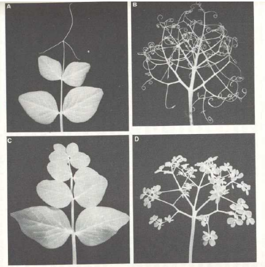

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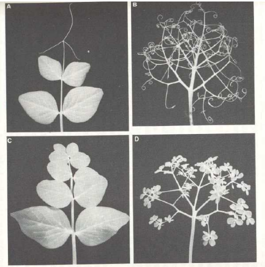

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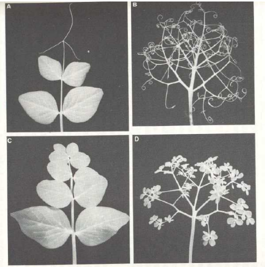

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- Changes in the switching are responsible for the mutants.

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The Developmental Cycle of Young's Model
Graphical Encapsulation of the Algebra

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$$\begin{array}{ccccc} & & S^{\ell} = KGS + C & & \\ & & \uparrow & & \\ S & \longrightarrow & GS & \longrightarrow & S^{c} = (1-2K)GS - 2C \\ & & \downarrow & & \\ & & S^{\ell} = KGS + C & & \end{array}$$

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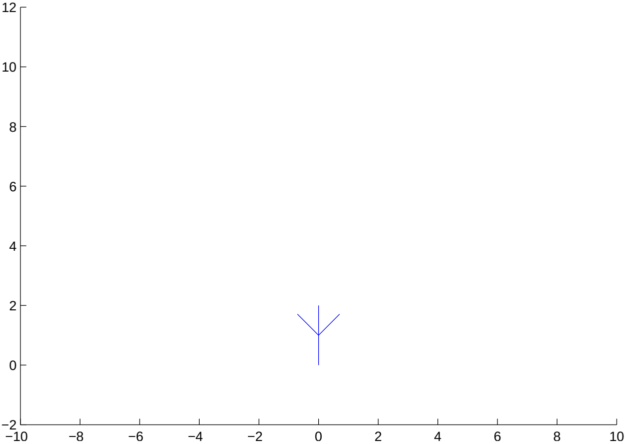
Switching to a different status is controled by Threshold Rules:

- if $S < T_1$, signal for switching to leaflet;
- if $S < T_2$, signal for switching to tendril.

Simulation of the Wild Type (normal pea leaf development)

Case A: $S_0 = 100, K = 0.1, C = 6, G = 1,$
$T_1 = 18, T_2 = 11$



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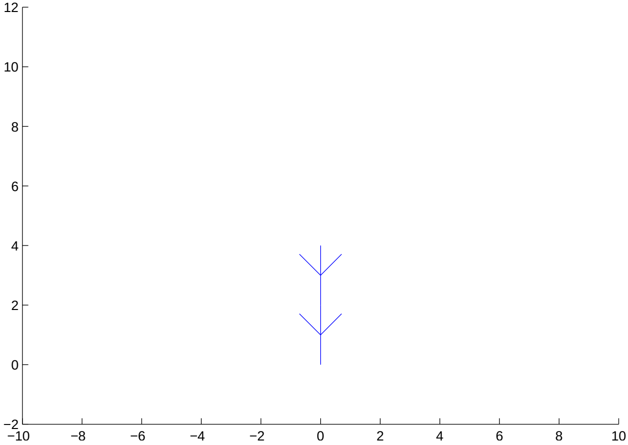

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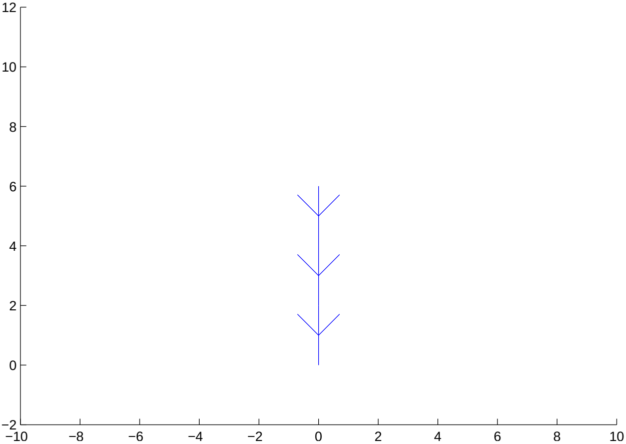

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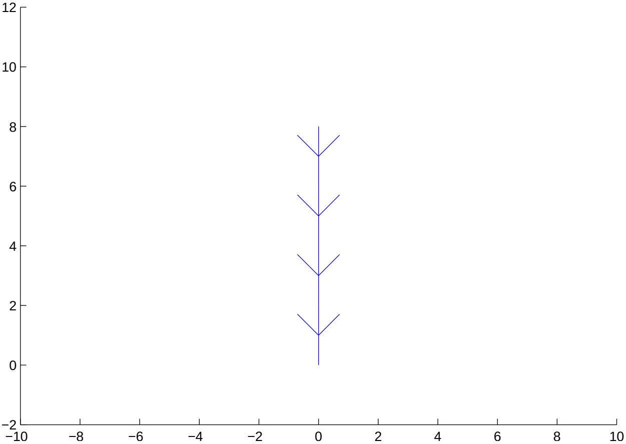

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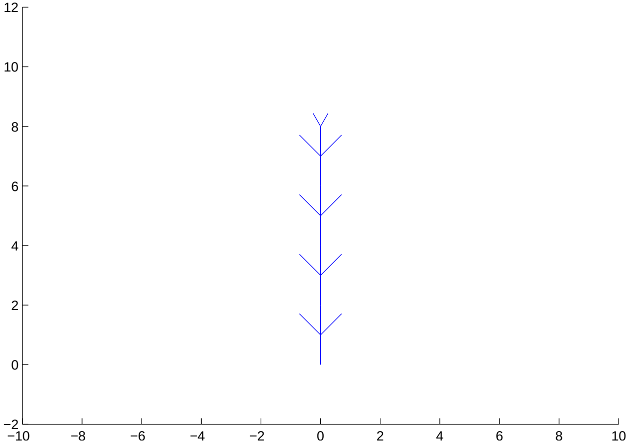

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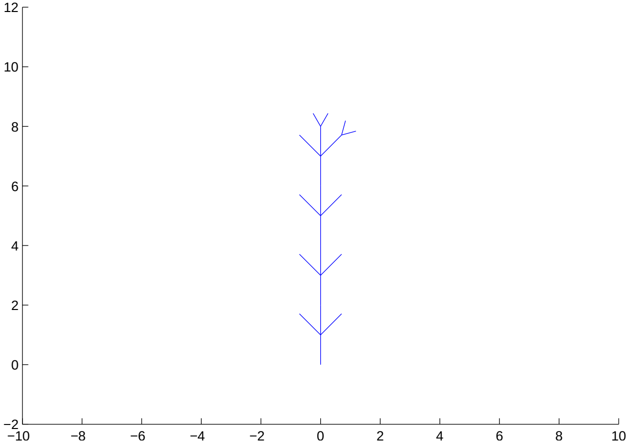

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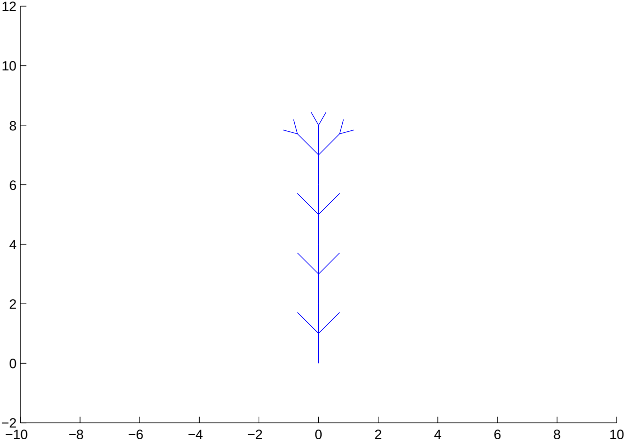

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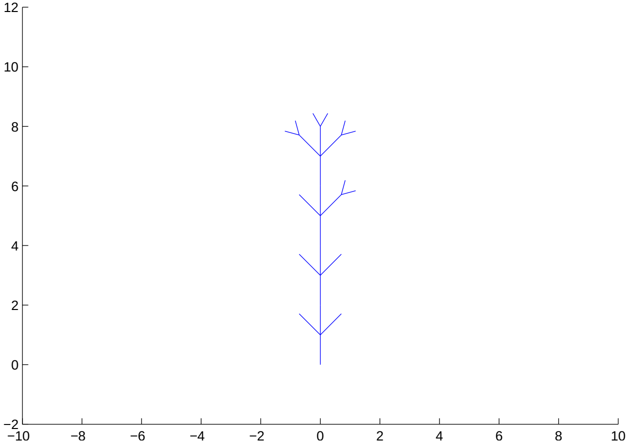

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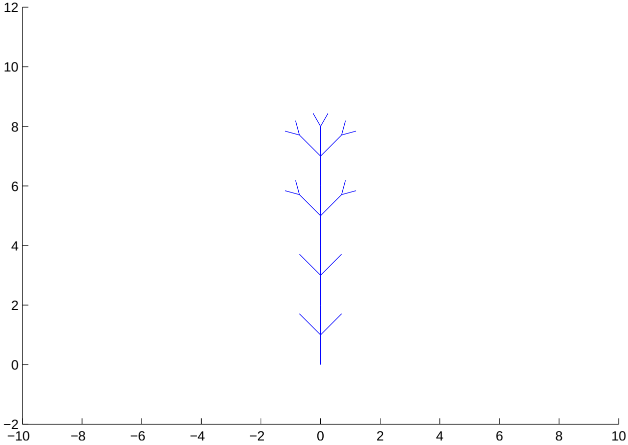

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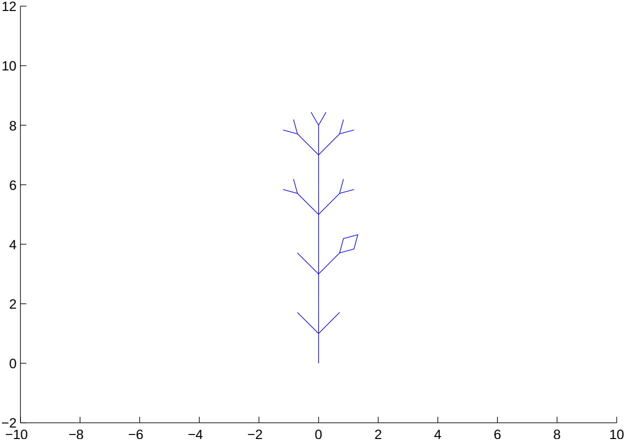

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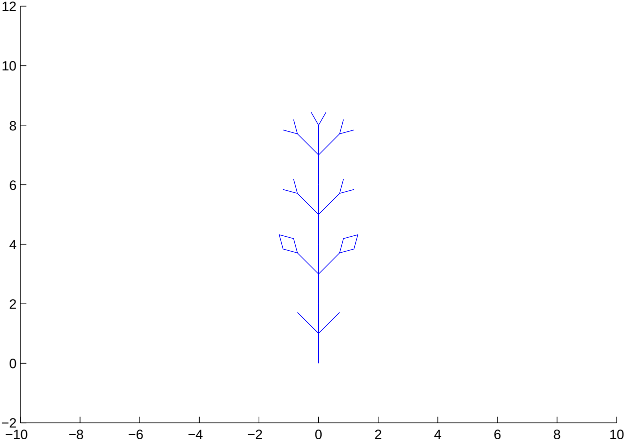

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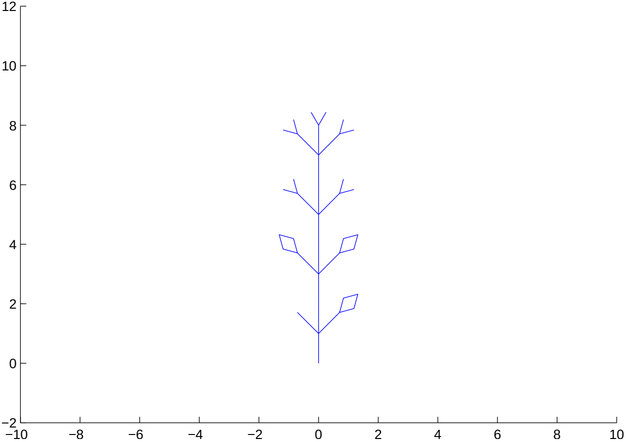

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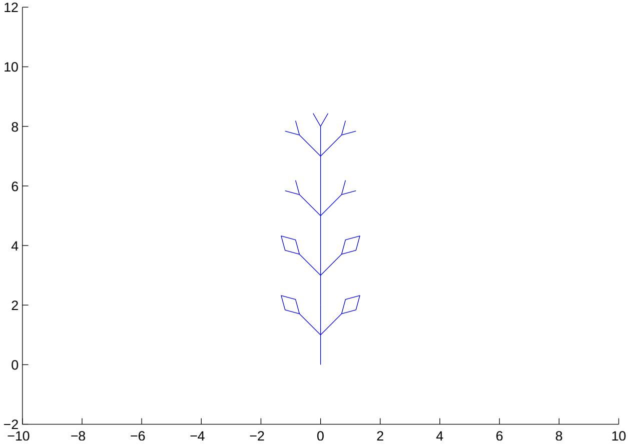

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Model Validation - the lesson learnt from Young (1983)

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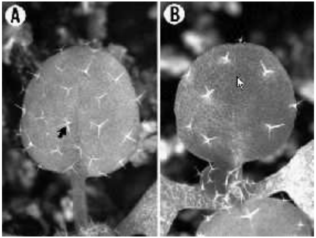
Biologically, the changes in the thresholds aim to model the switching occuring in the organism — trichomes (hairs) positioning on Arabidopsis leaves.



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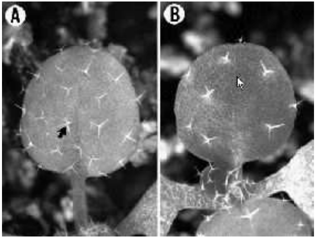

Larkin et al. (1996)

Such "signal accumulation and threshold switching"-modelling of a wild type and its mutant is a starting point for the identification of the actual switching occuring in the biological process being modelled.

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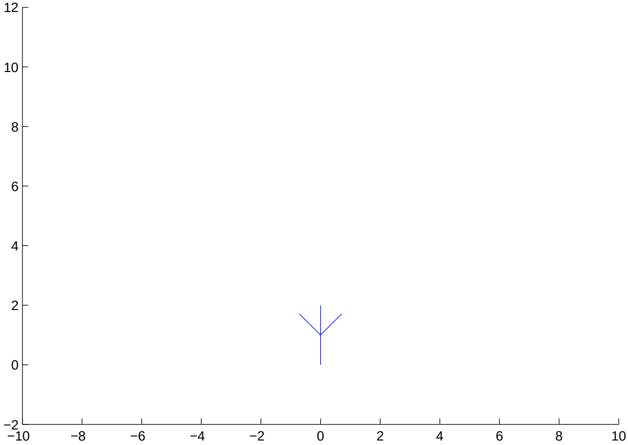

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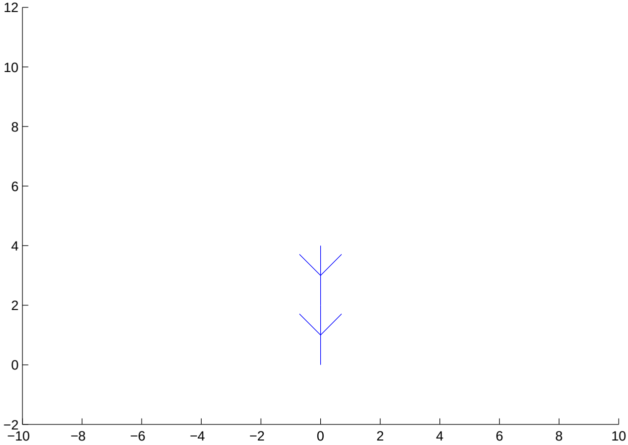

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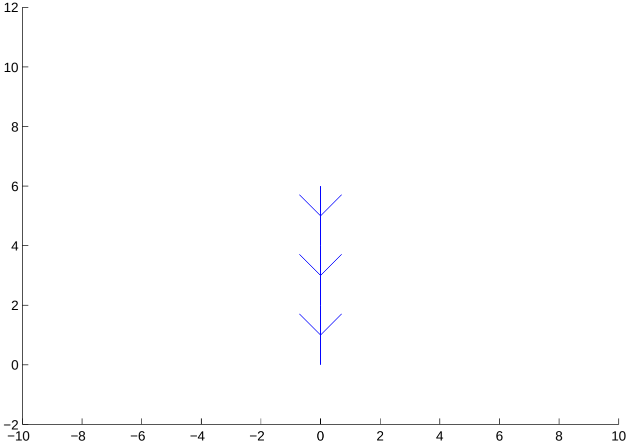

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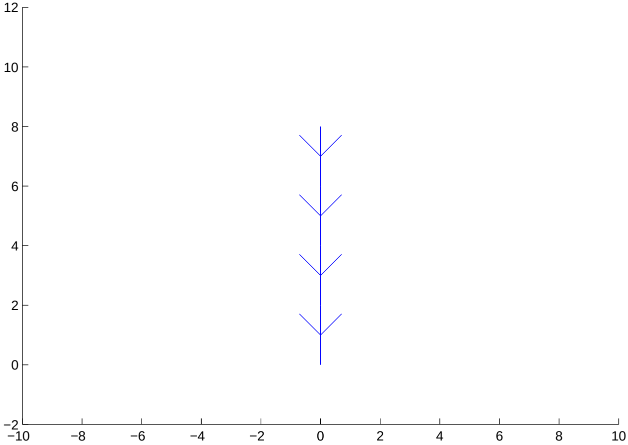

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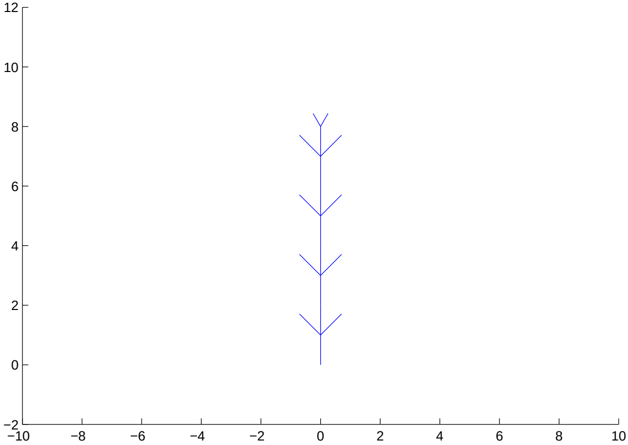

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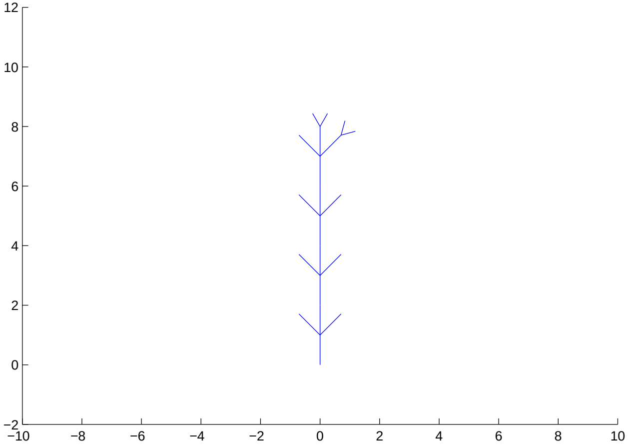

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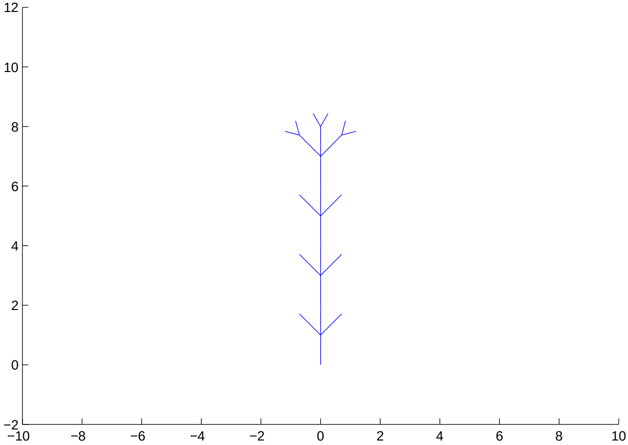

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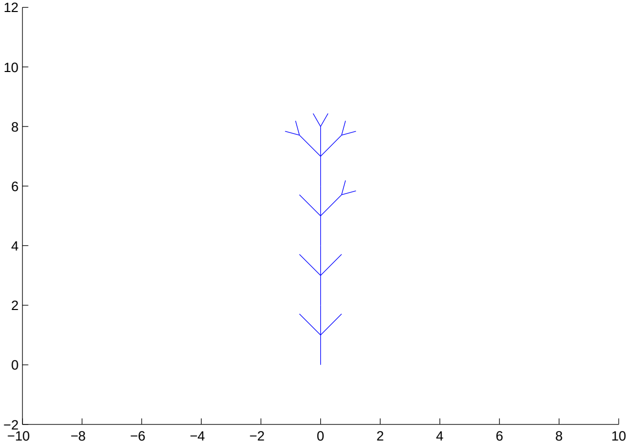

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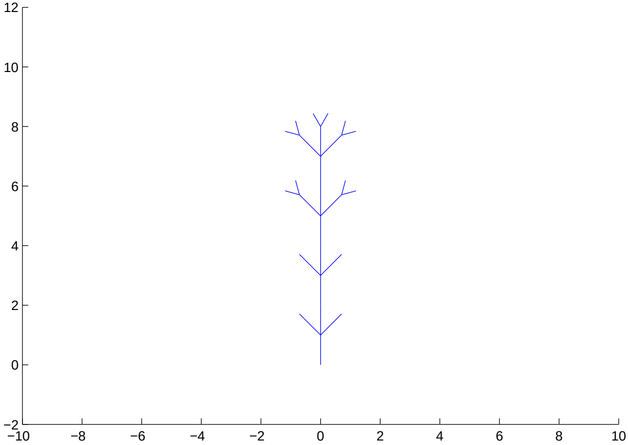

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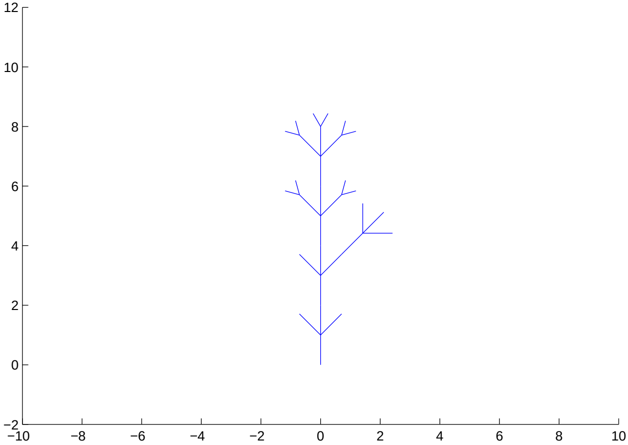

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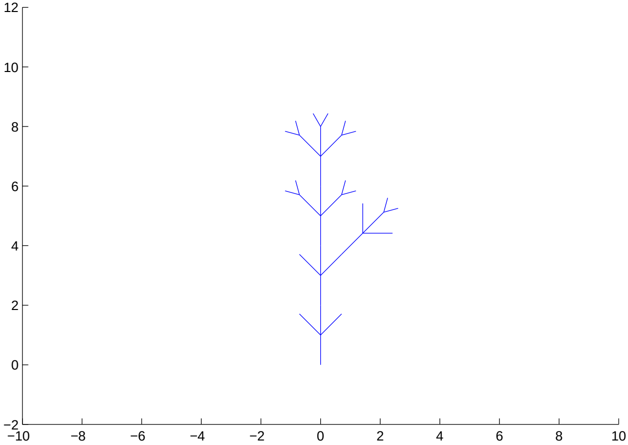

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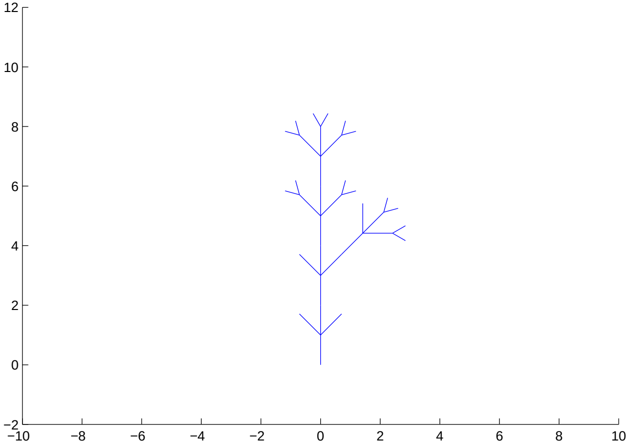

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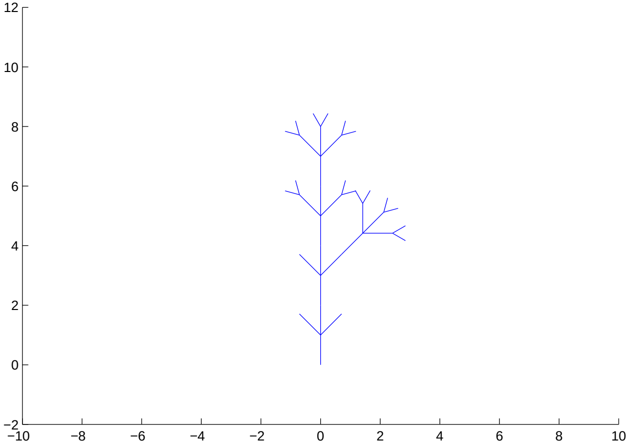

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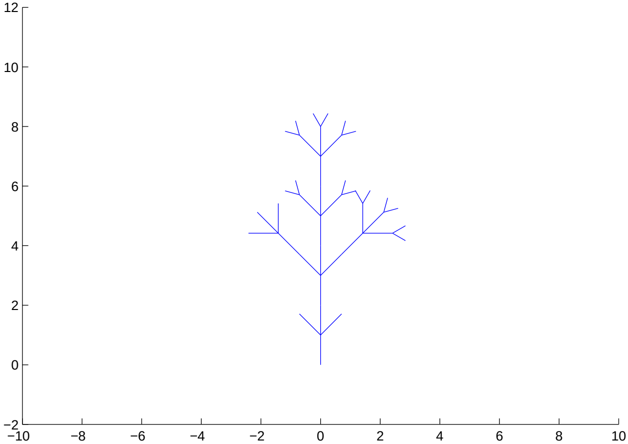

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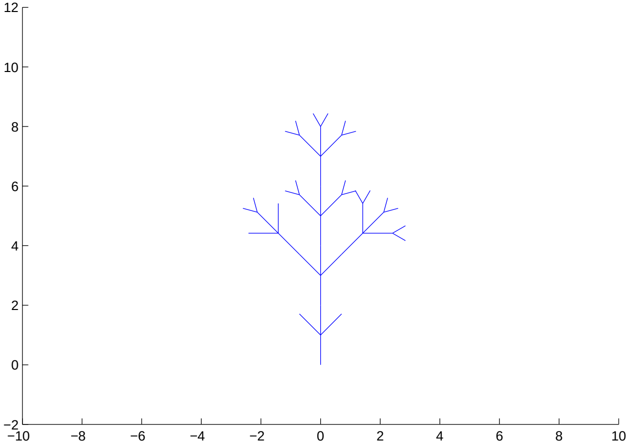

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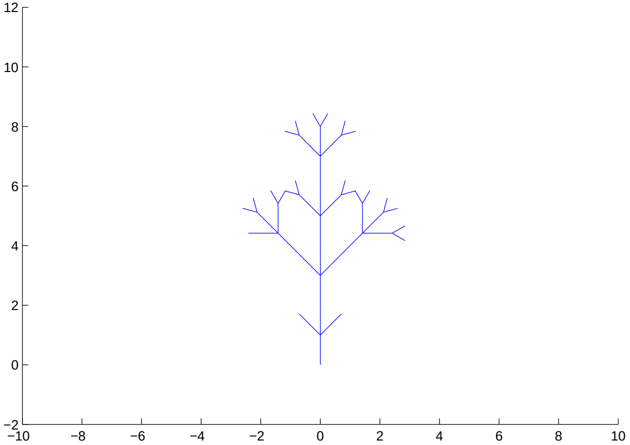

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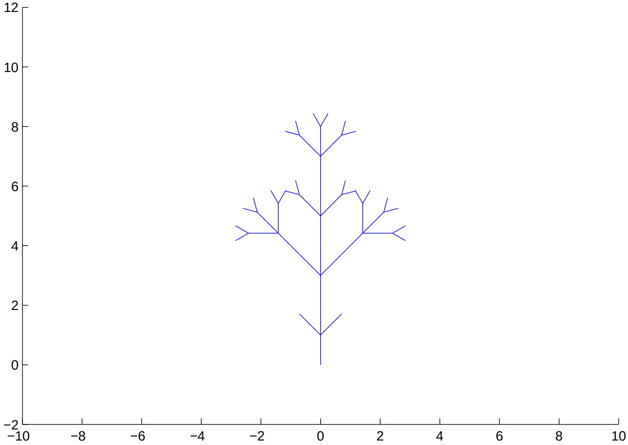

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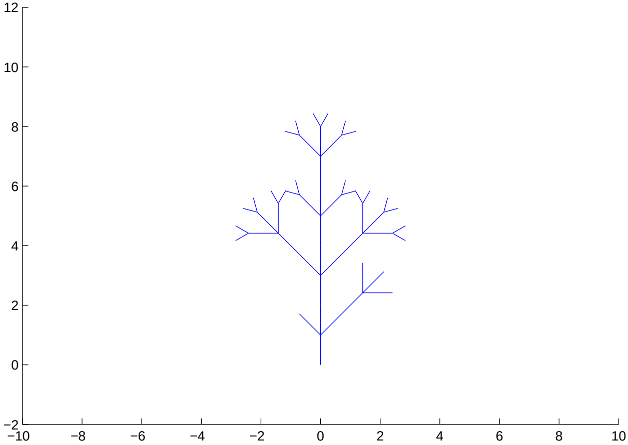

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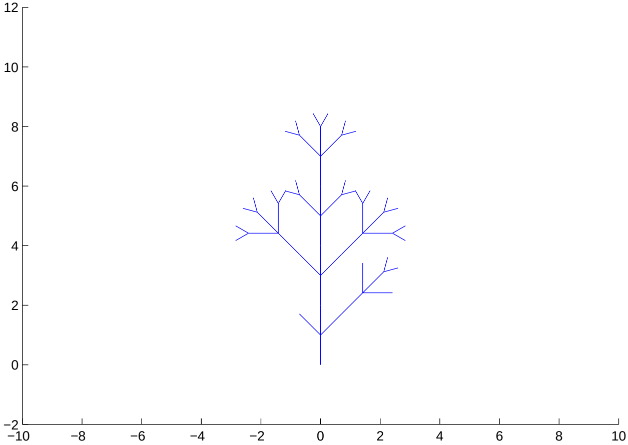

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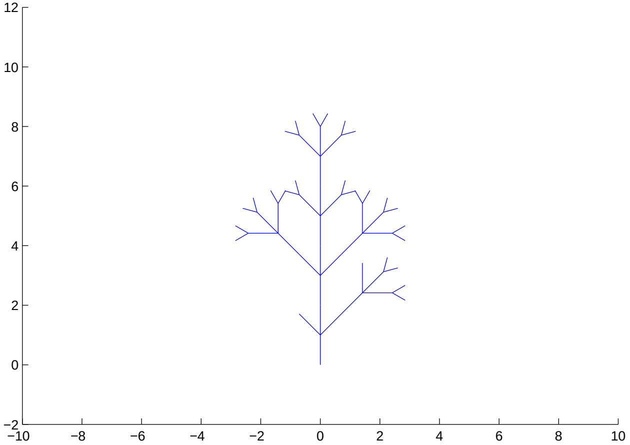

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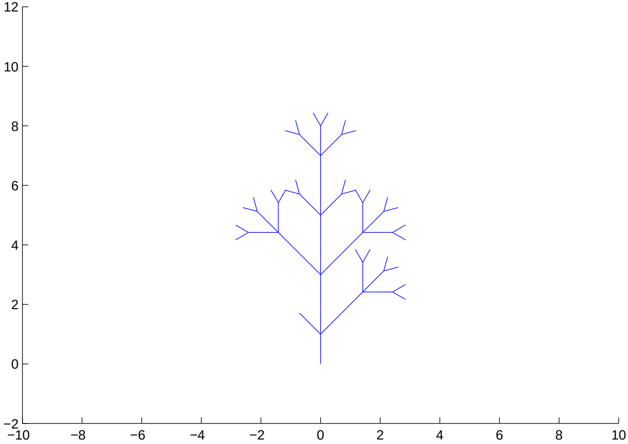

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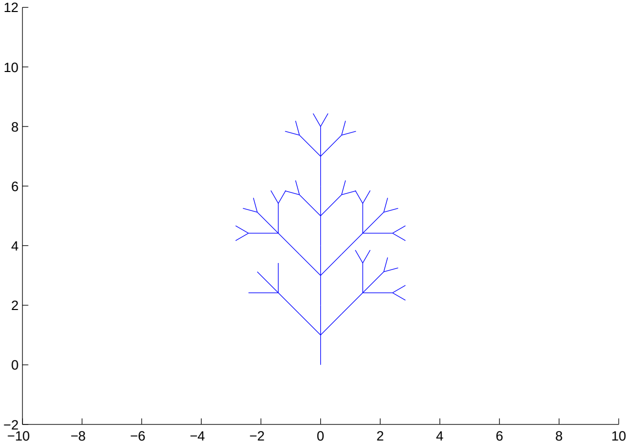

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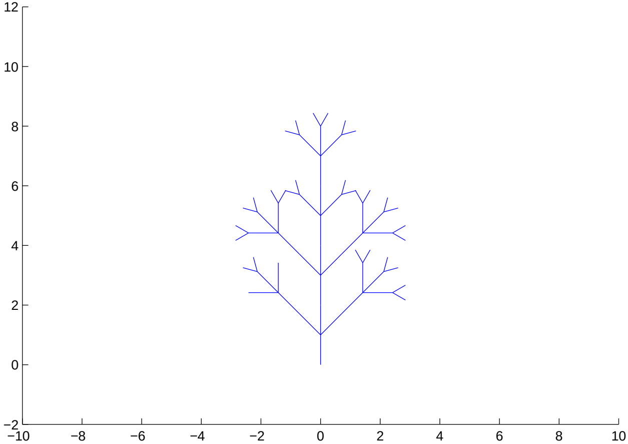

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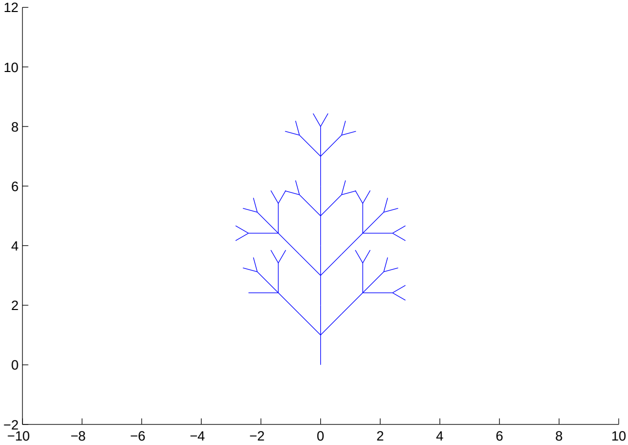

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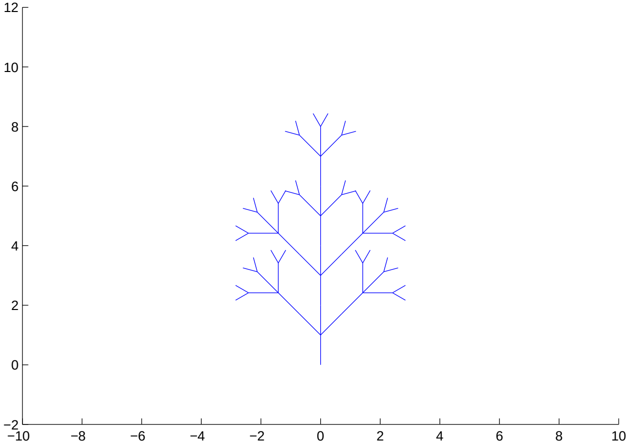

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Positional Information
Wolpert

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Leaf grows out of the embryo formed by the stem cells of the meristem with simultaneous trichome initiation in some cells and not others depending on the biological status of the forming cells.

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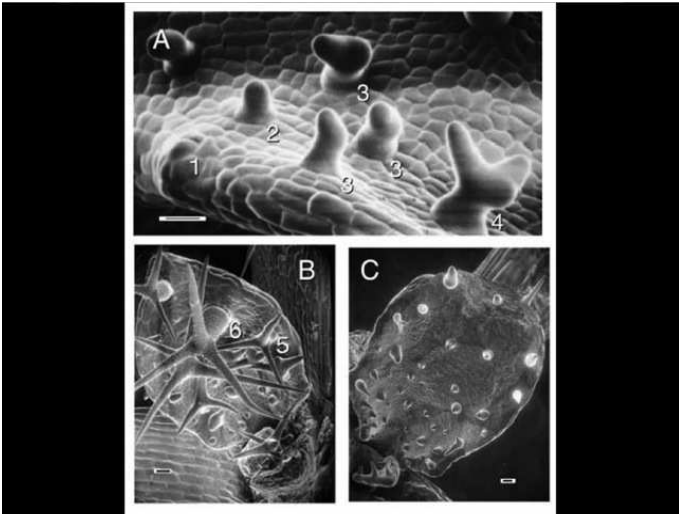
Notional Validation:
"One function of the shoot meristem may be to make tissue that can make leaves rather than to make leaves."

Poethig (1997)

Modelling Trichome Initiation During the Growth of the Leaf

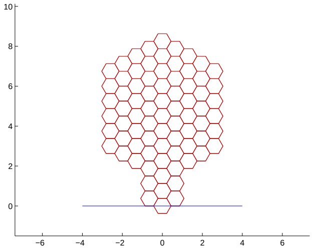


Lecture Notes, Jim Haseloff, Cambridge

Leaf Hexagonal Tile Geometry Representation

basic leaf module — hexagonal tile — collection of cells

Lateral versus Inner tiles



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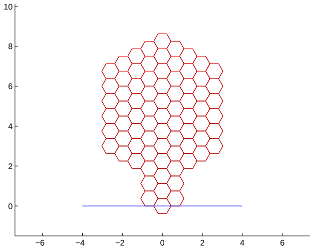


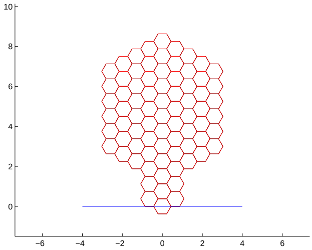
Algorithm:

- Procedure for growth from meristem.

Leaf Hexagonal Tile Geometry Representation

basic leaf module — hexagonal tile — collection of cells

Lateral versus Inner tiles



Algorithm:

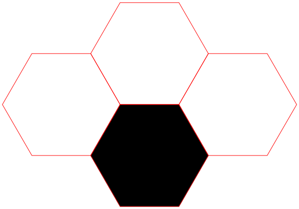
- Procedure for growth from meristem.
- Mechanism for communicating positional information $P(i, j)$.

- lateral tiles: $P(i, j) = 1$

The Local Hexagonal Signalling and Communication

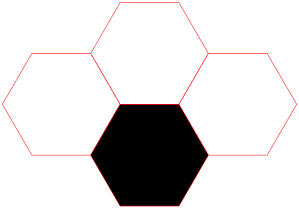
Mechanism for communicating positional information

- lateral tiles: $P(i,j) = 1$
- inner tiles:



$$P(i,j) = P(i-1, n_\ell) + P(i-2, n_c) + P(i-1, n_r)$$

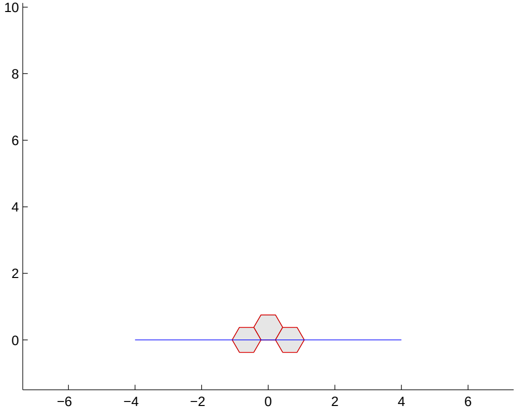
- lateral tiles: $P(i, j) = 1$
- inner tiles:



$$P(i, j) = P(i-1, n_\ell) + P(i-2, n_c) + P(i-1, n_r)$$

- if $P(i, j) \geq T$
  - trichome initiation
  - $P(i, j)$ of its neighbours below are reset to 1

An Example of a Simulation of Leaf Growth
Procedure for growth from meristem



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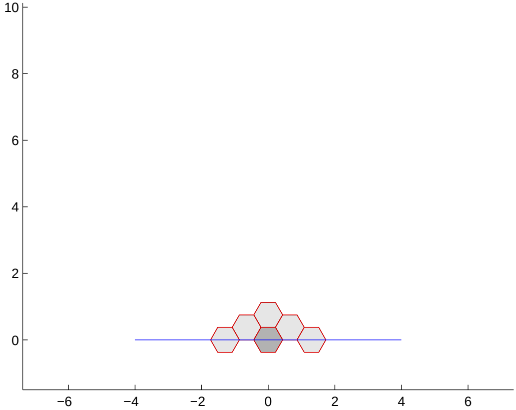
An Example of a Simulation of Leaf Growth
Procedure for growth from meristem



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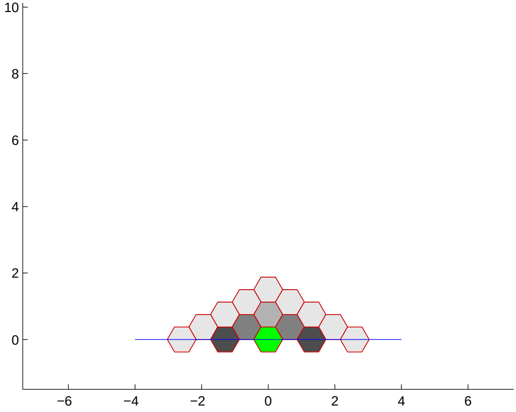
An Example of a Simulation of Leaf Growth

Procedure for growth from meristem



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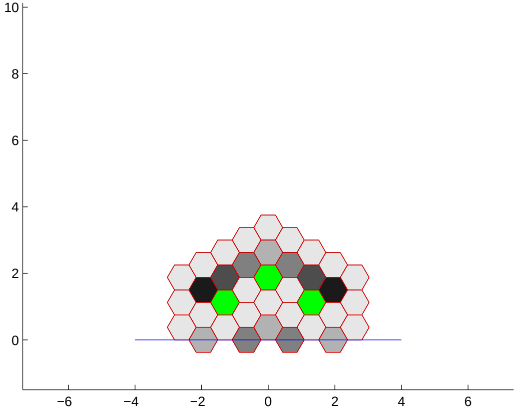

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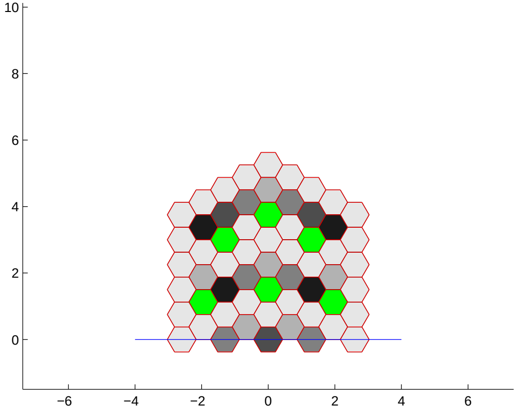
An Example of a Simulation of Leaf Growth
Procedure for growth from meristem



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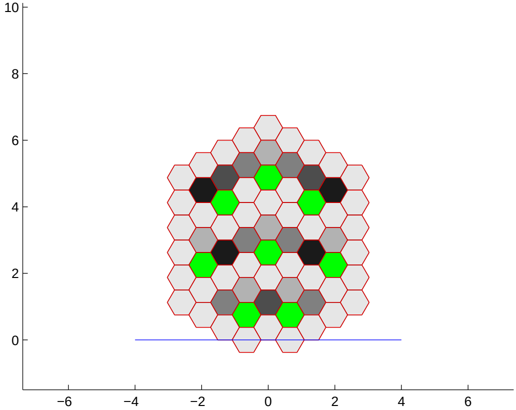
An Example of a Simulation of Leaf Growth

Procedure for growth from meristem



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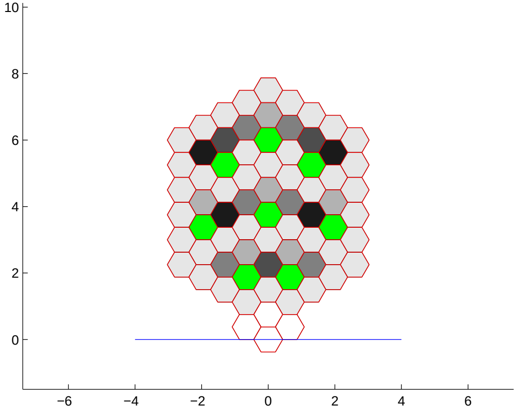
An Example of a Simulation of Leaf Growth

Procedure for growth from meristem



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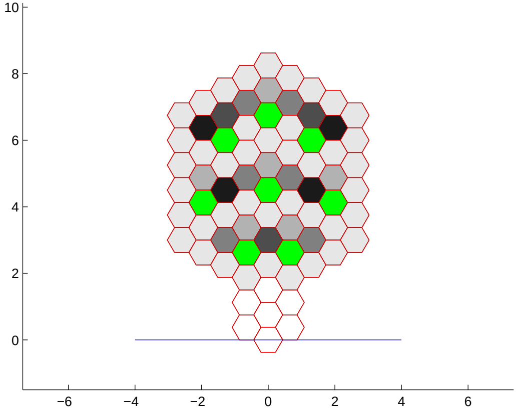
An Example of a Simulation of Leaf Growth
Procedure for growth from meristem



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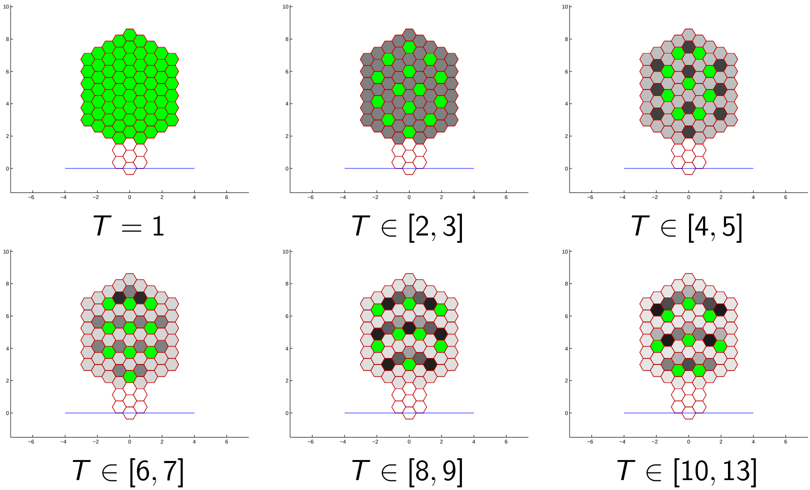
Various Patterns with different Thresholds



Simple Algebraic Modeling of Genetic Signalling, Communication and Switching

Proposed model is simple, but NOT its bio interpretation and math behavior

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- bio aspects — interpretations:
  - matching (iteratively) with the evolving genetics knowledge of known and new mutants [RICAM report];
  - explorative modeling (hypothesize, predict, modify).

Simple Algebraic Modeling of Genetic Signalling, Communication and Switching

Proposed model is simple, but NOT its bio interpretation and math behavior

- bio aspects — interpretations:
  - matching (iteratively) with the evolving genetics knowledge of known and new mutants [RICAM report];
  - explorative modeling (hypothesize, predict, modify).
- math aspects — behavior:
  - relationship between number of generated trichomes and values of threshold;
  - classification of possible trichome spatial distributions;
  - dependence on the total number of tiles.

Thank you!

Thank you!

In the applications of algebraic constructs
to the modelling of biological processes,
validation is not algebraic,
but the success
with which the algebraic ansatz
predicts observed biological behavior.