The leopard never changes its spots: realistic pigmentation pattern formation by coupling tissue growth with reaction-diffusion

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OVERVIEW

- Pigment formation
- Tissue growth
- Pattern enlargement
- Results
- Conclusions

sample code at mgmalheiros.github.io
We aim to realistically reproduce animal patterns
  - but we also want to get insights into the underlying biological processes
  - therefore, we look for a plausible explanation for pigmentation pattern formation
  - for that, we have explored the expressiveness of combining simple mechanisms
  - we have found that reaction-diffusion and tissue growth both play crucial roles
PIGMENT FORMATION

- Reaction-Diffusion (RD)
- Implementation
- Exploratory approach
REACTION-DIFFUSION

» OVERVIEW

- Pioneering work of Alan Turing
- Models autocatalytic chemical reactions
- PDEs involving two reagents $A$ and $B$:
  - $a$ and $b$ are local concentrations
  - there are reaction and diffusion parts
  - diffusion depends on nearby concentrations
  - $D_a$ and $D_b$ are the diffusion rates

\[
\frac{\partial a}{\partial t} = 16 - ab + D_a \nabla^2 a
\]

\[
\frac{\partial b}{\partial t} = ab - b - 12 + D_b \nabla^2 b
\]
REACTION-DIFFUSION

» DISCRETIZATION

- RD is typically solved by numerical methods
- Forward Euler integration is simple and fast
- The domain is a square lattice:
  - \(a\) and \(b\) are now two matrices
  - \(\nabla^2 a\) and \(\nabla^2 b\) are the Laplacian operators, implemented by finite differences
  - we use a 9-point stencil, with the given weights around a center cell

\[
\Delta a = (16 - ab + D_a \nabla^2 a) \Delta t
\]

\[
\Delta b = (ab - b - 12 + D_b \nabla^2 b) \Delta t
\]
First, define the initial values for $a$ and $b$

Given $\Delta t$, loop until a final time is reached

At each iteration:
- compute Laplacians for all matrix elements
- evaluate $\Delta a$ and $\Delta b$
- calculate $a_{next}$ and $b_{next}$
- limit $a_{next}$ by lower bound $L_a$ and upper bound $U_a$
- limit $b_{next}$ by lower bound $L_b$ and upper bound $U_b$

$$a_{next} = a + \Delta a$$
$$b_{next} = b + \Delta b$$

$$a = \text{clip} \left( a_{next}, L_a, U_a \right)$$
$$b = \text{clip} \left( b_{next}, L_b, U_b \right)$$
REACTION-DIFFUSION

» INITIAL CONDITIONS

• Reaction-diffusion is sensitive to initial values

• However, pattern formation is also robust:
  - small perturbations yield small pattern changes
  - a fixed set of parameters induces the same resulting pattern structure, despite the randomness

• For most experiments we use:
  - \( a_{\text{initial}} = 4 \)
  - \( b_{\text{initial}} = 4 + \text{uniform random noise in } [0, 1] \)
We employ two types of boundaries:

- toroidal wrapping → matrix borders wrap around

- no-flux boundary → matrix borders have their concentrations extended outward
The Turing model exhibits cross kinetics, that is, A and B are completely out of phase.

For display:
- we typically map either the $a$ or $b$ matrices to a perceptually-uniform color map
- some experiments also use a simple linear-interpolated color map
- no further alteration
EXPLORATORY APPROACH

» PARAMETERS

- We have explored the parameter space of the original model, and then proposed extensions to improve expressibility and usage:
  - let $D_a = rs$ and $D_b = s$
  - $r$ is the ratio between diffusion rates → structure
  - $s$ expresses the overall pattern scale
  - previously $L_b = 0$, but we found that positive values also alter the pattern structure
  - setting $U_a$ and $U_b$ also changes the dynamics
EXPLORATORY APPROACH

» PARAMETER MAPS

ratio \(x \times U_a(y)\)

ratio \(x \times L_b(y)\)
TISSUE GROWTH

- Static and growing domains
- Matrix expansion
- Effect of growth
Static Domain

- Normal Turing patterns present a space-filling behavior
- Patterns tend to create equispaced features:
  - spots
  - stripes or labyrinths
  - a mix of both
- The average distance between features is called the pattern wavelength
GROWING DOMAIN

» TWO PREVIOUS APPROACHES

• #1 Add continuous growth term to PDEs:
  − simulation still runs over a square lattice
• #2 A point-based cellular model, following the biologic analogy:
  − diffusion occurs only among nearby cells
  − cells divide and push others
• The drawback is being expensive:
  − needs collision mechanics
  − needs repeated Nearest Neighbor Search
Here we propose *matrix expansion*:
- we approximate uniform growth by randomly selecting matrix elements and duplicating them
- this is performed once for each row → yields a new column
- then it is performed once for each column → yields a new row

The domain is always a regular matrix:
- on average, cell divisions are uniformly spread
- we define a *growth rate* during simulation
EFFECT OF GROWTH

» INITIAL STATE

Only growth
reagent B

1
EFFECT OF GROWTH

» ONLY GROWTH, NO DIFFUSION
EFFECT OF GROWTH

» GROWTH AND REACTION-DIFFUSION
EFFECT OF GROWTH

» GROWTH AND SATURATED REACTION-DIFFUSION

Saturated RD and growth

reagent B

5000
PATTERN ENLARGEMENT

- Problem
- Continuous reinforcement
- Effect of growth
PROBLEM

• How to maintain the overall pattern appearance during growth?
  - cell division adds noise!
  - large constant areas need to expand
  - borders must be kept well-defined: sharp, not blurry

• Reaction-diffusion does not have these properties, but a similar model can achieve this
Continuous Reinforcement

- Models an autocatalytic reaction
- Has a dual effect: smoothing and maintenance
- PDE involving reagent C:
  - $c$ is the local concentration
  - there are reaction and diffusion parts
  - diffusion depends on nearby concentrations
  - $D_c$ is the diffusion rate

\[
\frac{\partial c}{\partial t} = \gamma (t - w - c)(t - c)(t + w - c) + D_c \nabla^2 c
\]
CONTINUOUS REINFORCEMENT

GROWTH AND REINFORCEMENT

Only reinforcement
reagent A

2000
RESULTS

- Impact of initial state
- Simulated biologic patterns
RESULTS

PREPATTERN

- The initial state of the simulation is called a *prepattern*.
- We employed two types of prepatterns:
  - random initial concentration
  - local random production
- Simulations have two or more phases.
- The resulting concentrations of a phase are directly fed into the next phase.
RESULTS

» RANDOM INITIAL CONCENTRATION

- Prepattern:
  - reagent A starts constant
  - reagent B starts constant plus a small random variation
- The first phase usually develops into spots
- Many works state the ubiquity of spots in early embryonic development
RESULTS

» RETICULATE WHIPRAY

Reticulate whipray
reagent B

photo by Brian Gratwicke (Flickr, CC BY 2.0)
RESULTS

» RETICULATE WHIPRAY

Reticulate whipray
reagent B

14000

photo by Brian Gratwicke (Flickr, CC BY 2.0)
RESULTS

» HONEYCOMB WHIPRAY

Honeycomb whipray reagent B

photo by the authors
RESULTS

» HONEYCOMB WHIPRAY

Honeycomb whipray
reagent B

24000

photo by the authors
RESULTS

» YELLOW-BANDED POISON DART FROG

Yellow-banded poison dart frog

reagent A

| 20 |

photo by Adrian Pingstone (Wikimedia Commons, public domain)
RESULTS
» YELLOW-BANDED POISON DART FROG

Yellow-banded poison dart frog
reagent A

19000

photo by Adrian Pingstone (Wikimedia Commons, public domain)
RESULTS

» LOCAL RANDOM PRODUCTION

- Prepattern:
  - reagent A starts constant
  - reagent B starts constant
  - B is produced in small random amounts, along the dorsal spine

- The first phase usually develops into straight stripes

- Growth noise disrupts the stripes in very interesting ways
RESULTS

» THIRTEEN-LINED GROUND SQUIRREL

Thirteen-lined ground squirrel
reagent B

photo by Mnmazur (Wikimedia Commons, public domain)
RESULTS

» THIRTEEN-LINED GROUND SQUIRREL

Thirteen-lined ground squirrel

reagent B

16000

photo by Mnmazur (Wikimedia Commons, public domain)
RESULTS

» LEOPARD

Definition phase: only reaction-diffusion, no growth

A

B

C

100

photo by Derek Keats (Flickr, CC BY 2.0)
RESULTS

» LEOPARD

Maintenance phase: only reinforcement, slow growth

A

B

C

242000

photo by Derek Keats (Flickr, CC BY 2.0)
RESULTS

» LEOPARD

• With a single set of parameters:
  - stripes develop into spatially-organized spots
  - due to growth, spots split into rosettes
  - limited growth in the dorsal spine produces deformed rosettes
  - shorter growth phases provide continuous variation of rosettes on other parts of the body

photo by Derek Keats (Flickr, CC BY 2.0)
RESULTS

» LEOPARD

• Important insights:
  - the residual pattern before growth provides the brown spots
  - pheomelanin (reddish pigment) and eumelanin (black pigment) are induced by the same process

• 3D rendering:
  - simple mapping from final concentrations to pigmentation, using a specialized fur shader
  - visual complexity arises from fur orientation and self-shading
CONCLUSIONS

- Contributions
- Future work
CONCLUSIONS

- Tissue growth can be successfully approximated by matrix expansions
- The extended RD model provides great expressiveness and more intuitive controls
- A continuous reinforcement equation is demonstrated
- We emphasize the importance of the careful definition of the initial state
- We have generated a few unprecedented 2D patterns matching real species
CONCLUSIONS

» FUTURE WORK

- Simulate pigment formation over a developing 3D surface
- Evaluate other mechanisms to couple geometric modification and localized pattern change
- Provide a deeper mathematical analysis
- Implement an artist-oriented pipeline for pattern design
- Develop a technique for pattern similarity comparison and visual characterization, able to automate classification and recognition
- Perform new experiments to reproduce more species
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