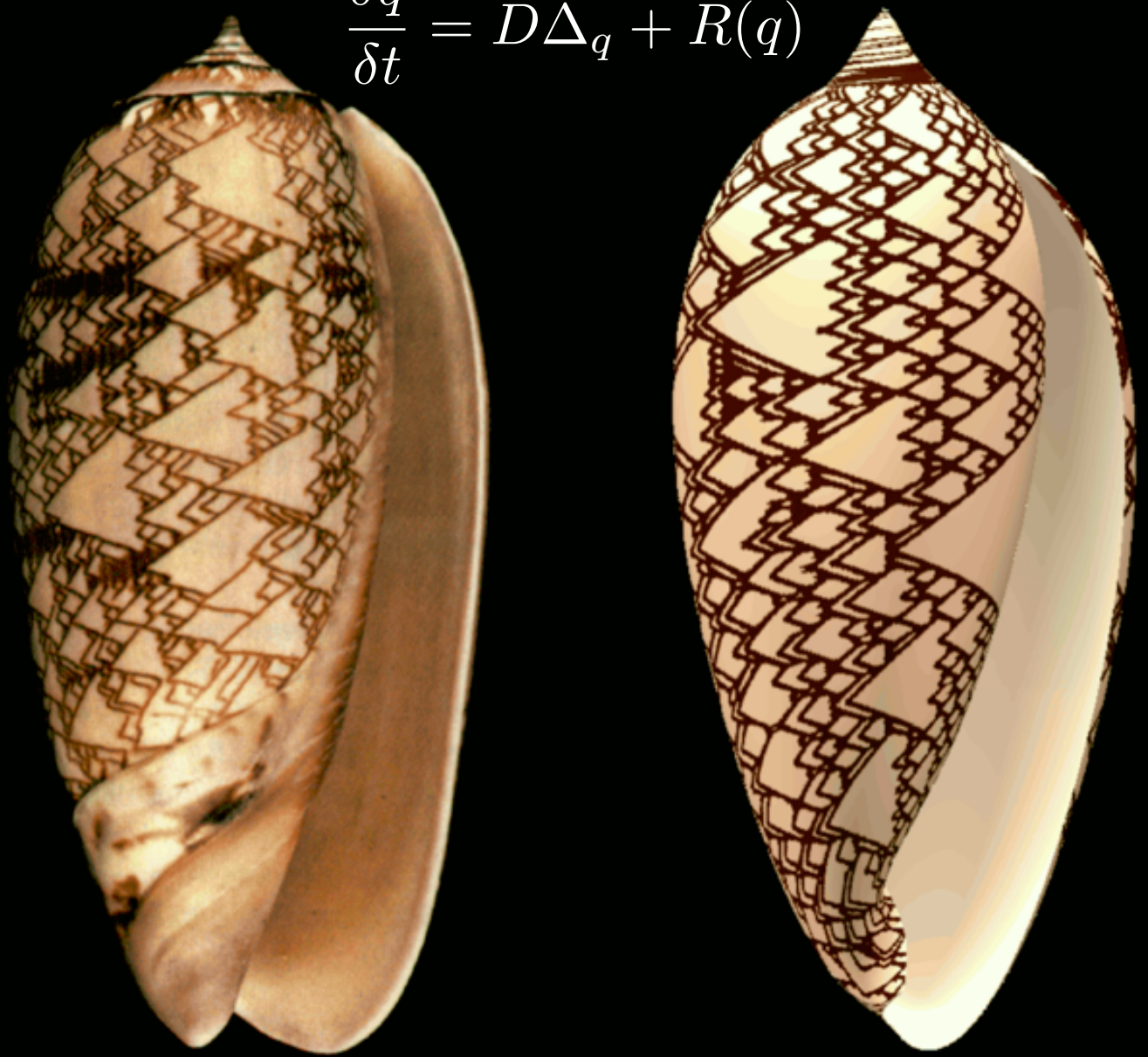
Reaction-Diffusion

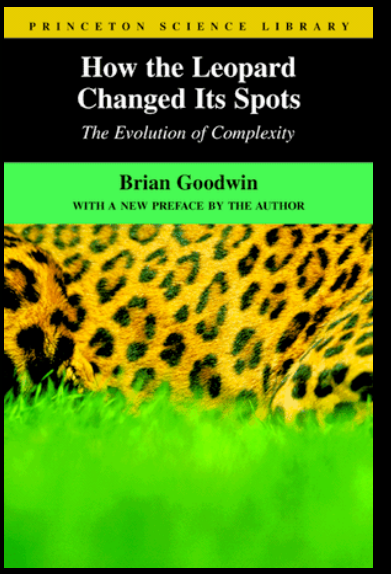
Introducció a la Universitat: Física

Javier Macia & Sergi Valverde

The Algorithmic Beauty of Seashells

$$\frac{\delta q}{\delta t} = D\Delta_q + R(q)$$

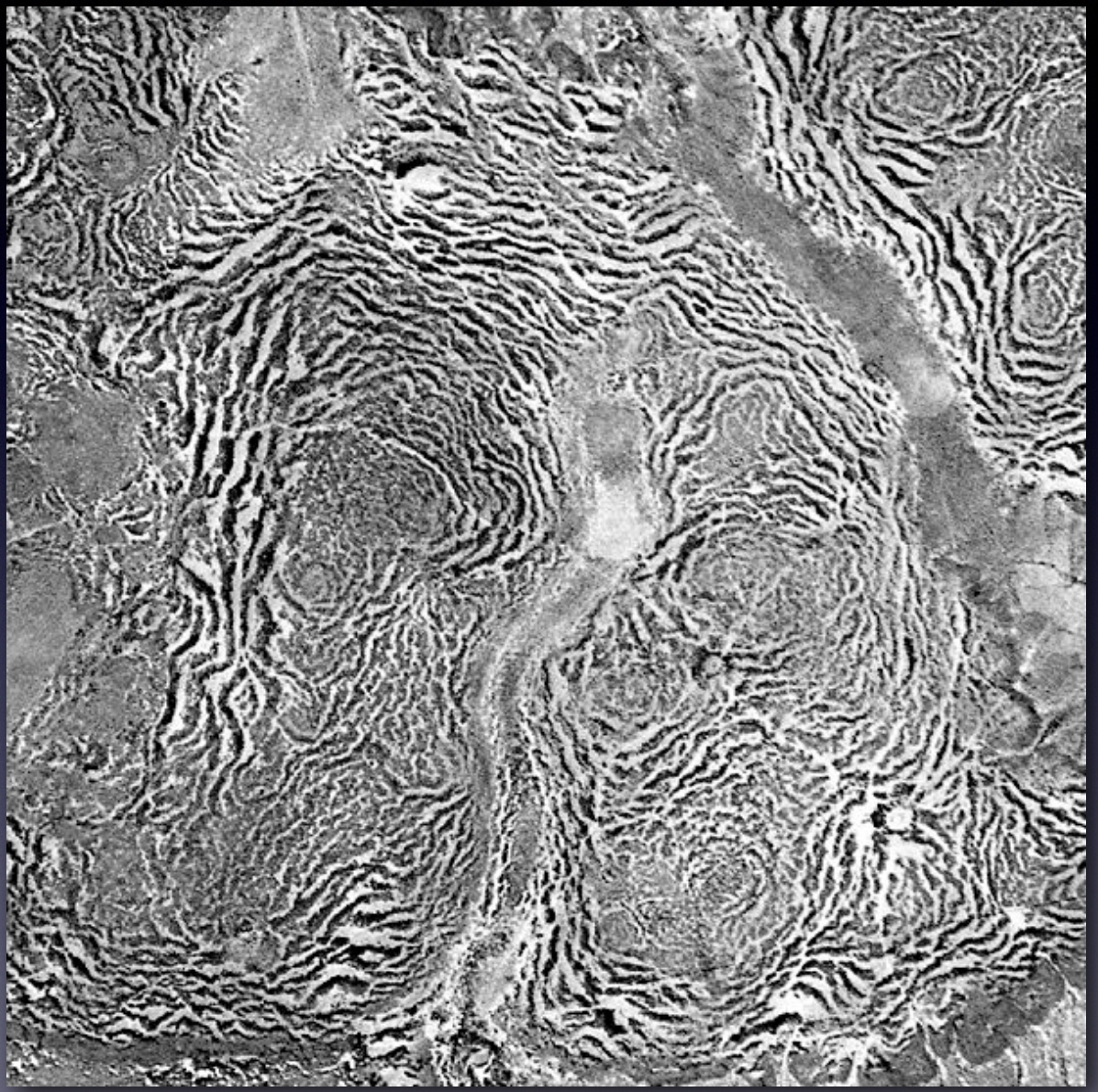




A. M. Turing, The **chemical basis** of **morphogenesis'**, Philosophical Transactions of the Royal Society of London , Series B, No.641, Vol. 237, 14 August (1952)

Pattern formation in Ecology

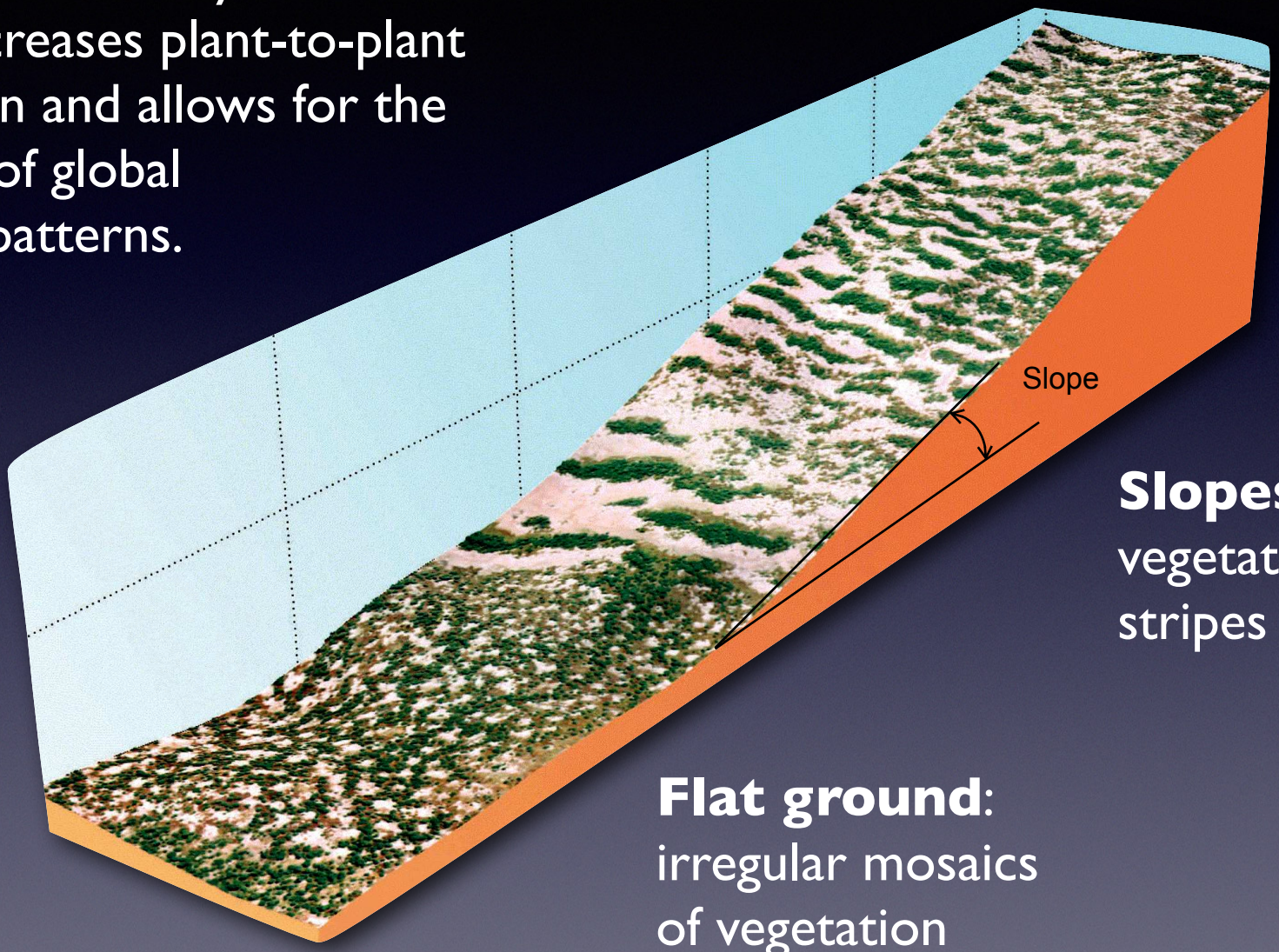
Tiger bush: distance between bands 60-120 m



5 x 5 km (Niger)

Pattern formation in Ecology

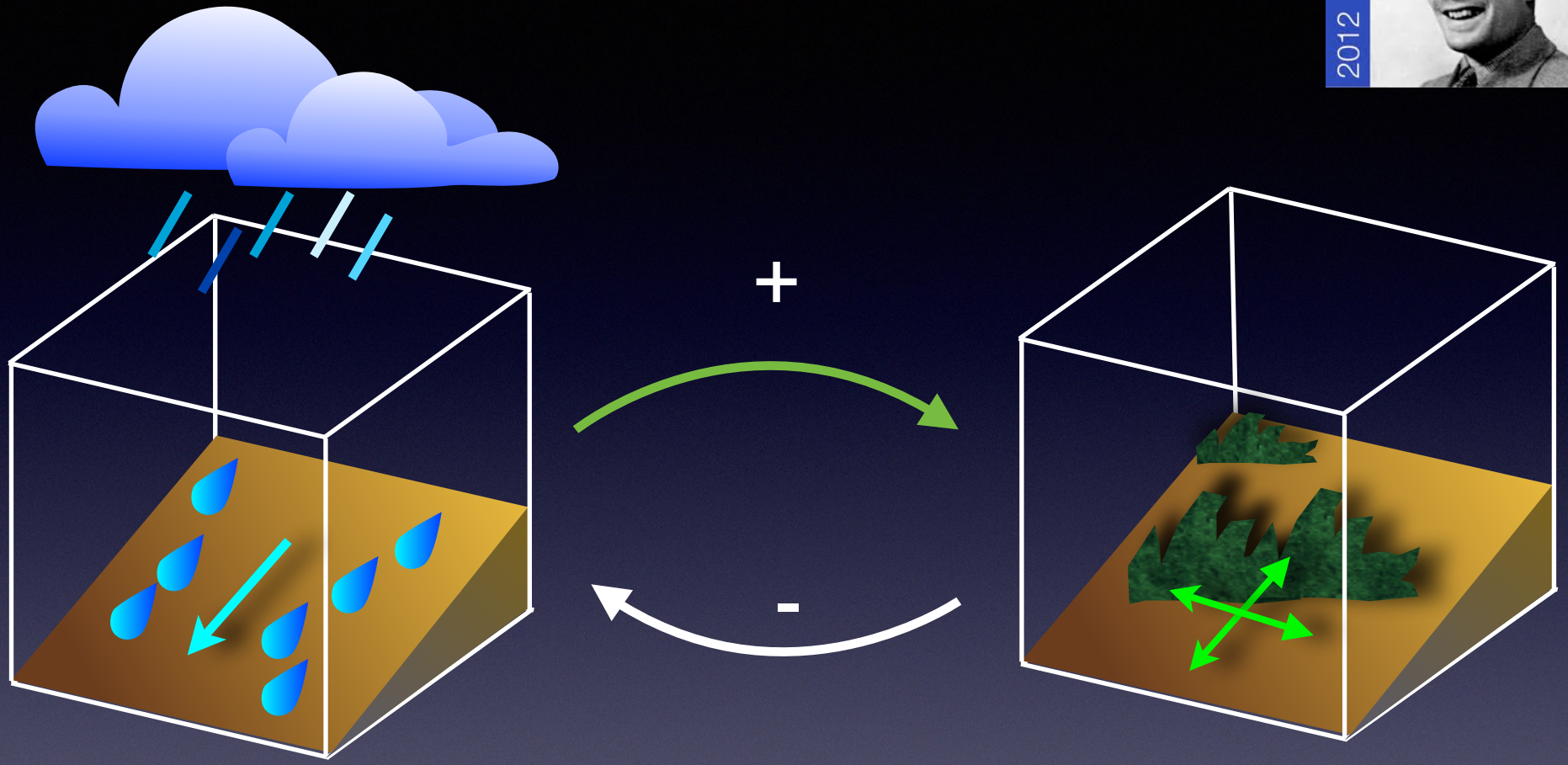
Adaptation of root systems to water scarcity increases plant-to-plant competition and allows for the formation of global landscape patterns.



Slopes: vegetation stripes

Flat ground: irregular mosaics of vegetation

Mathematical Model of Klausmeier

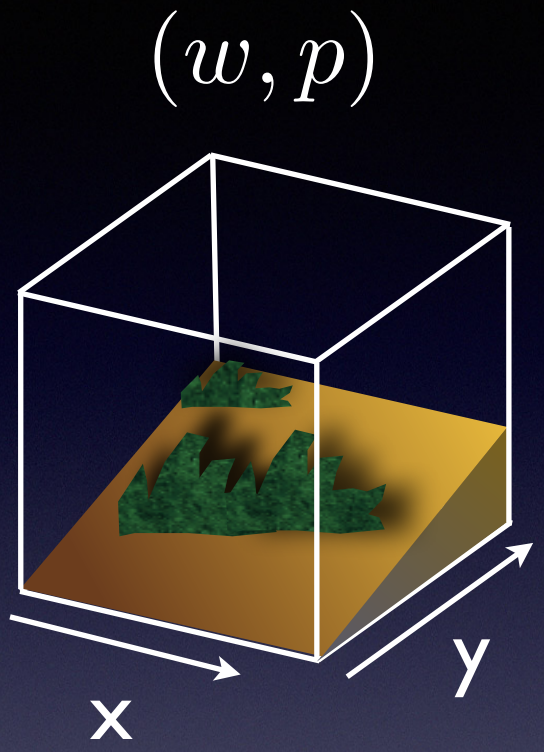


Rate of change of water

Rate of change of plant

C. A. Klausmeier, "Regular and Irregular Patterns in Semiarid Vegetation"
Science 284(5412), pp. 1826–1828 (1999)

Mathematical Model of Klausmeier



Rate of change of water = Rainfall - Uptake by plants - Flow downhill

$$\frac{dw}{dt} = a - wp^2 + v\frac{dw}{dy}$$

Rate of change plant biomass = Growth, proportional to water uptake - Mortality - Random dispersal

$$\frac{dp}{dt} = wp^2 - mp + D\left(\frac{d^2p}{dx^2} + \frac{d^2p}{dy^2}\right)$$

C. A. Klausmeier, "Regular and Irregular Patterns in Semiarid Vegetation"
Science 284(5412), pp. 1826–1828 (1999)

Qüestió 1: Implementar el model del "tiger bush"

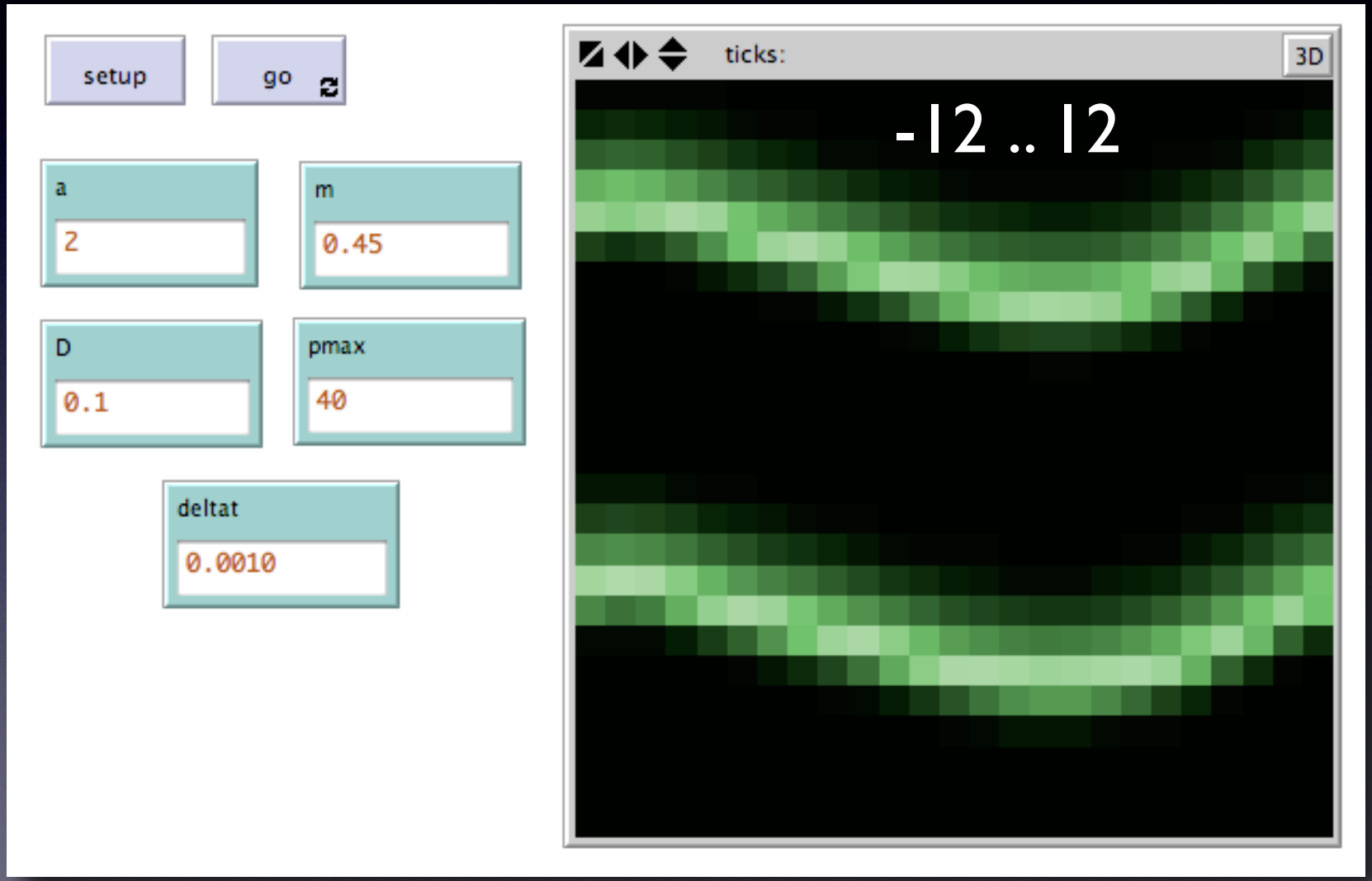
$a = 2$

$m = 0.45$

$D = 0.1$

$p_{max} = 40$

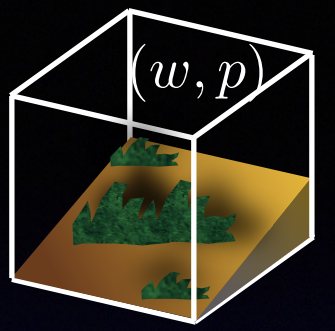
$\Delta t = 0.001$



to setup

```
globals [ v ]
patches-own [  w  p deltap deltaw  ]
to setup
   clear-all
   set v 182.5
   let peq  0.5 *  ( a / m +  sqrt ( ( a / m ) * ( a / m ) - 4 ) )
   let weq  m / peq
   ask patches
   [
      set p peq + 0.1 * random-float 1
      set w weq + 0.1 * random-float 1
   ]
   ask patches
   [
      set pcolor scale-color green p 0 pmax
   ]
end
```

to go



1) Integrar equacions diferencials (Euler)

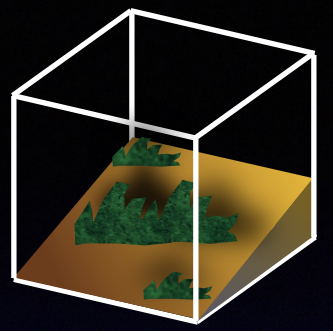
$$\frac{dw}{dt} = a - wp^2 + v\frac{dw}{dy} \longrightarrow \text{deltaw}$$

$$\frac{dp}{dt} = wp^2 - mp + D\left(\frac{d^2p}{dx^2} + \frac{d^2p}{dy^2}\right) \longrightarrow \text{deltap}$$

2) Assegurar que les concentracions son sempre positives!

```
ask patches
[
      if w < 0 [ set w 0 ]
      if p < 0 [ set p 0 ]
]
```

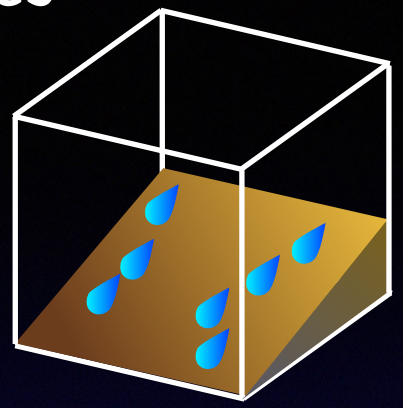
to go



3) Pintar el *patch* de color verd amb escala de colors proporcional a la variable 'p' (`scale-color`)

```
ask patches
[
  set pcolor scale-color green p 0 pmax
]
```

Integració de la concentració d'aigua als *patches*



```
to go
  ask patches
  [
       ; per a cada patch (x,y) calcular  deltap i deltaw
```

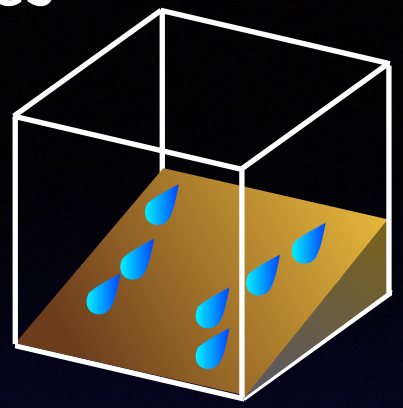
$$\frac{dw}{dt} = a - wp^2 + \nu \frac{dw}{dy}$$

$$\frac{dp}{dt} = wp^2 - mp + D\left(\frac{d^2p}{dx^2} + \frac{d^2p}{dy^2}\right)$$

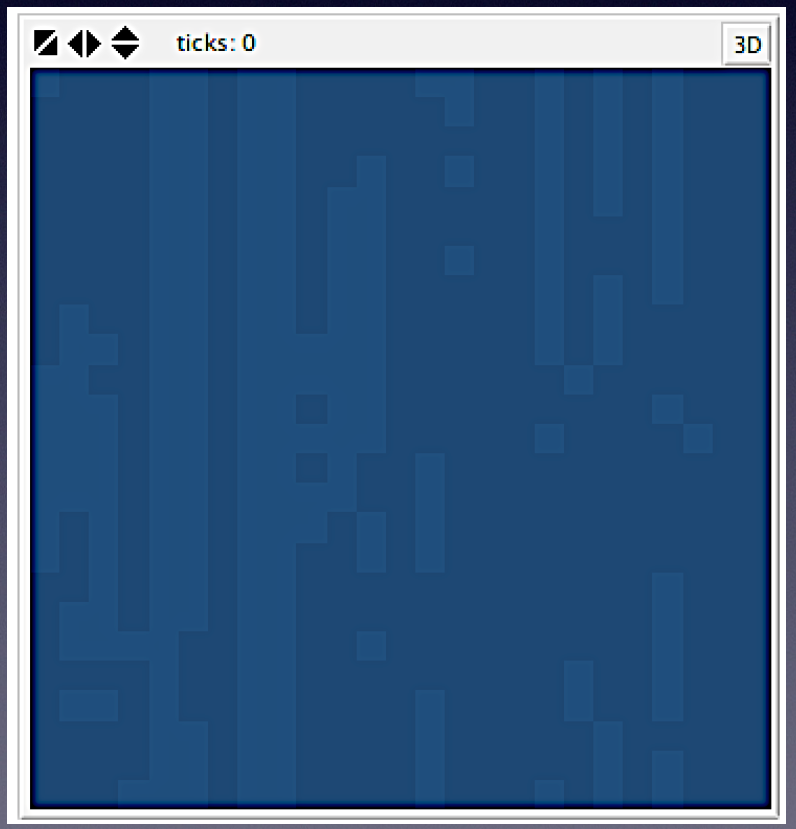
→ `set deltap 0`

```
  ]
  ask patches
  [
       set w  w + deltat * deltaw
       set p  p + deltat * deltap
       if w < 0 [ set w 0 ]
       if p < 0 [ set p 0 ]
  ]
   ask patches
   [
      set pcolor scale-color blue w 0 1
   ]
end
```

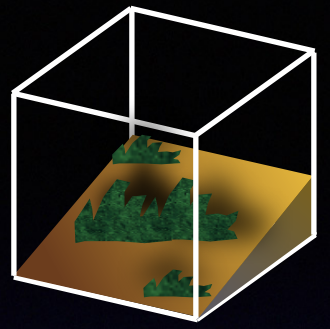
Integració de la concentració d'aigua als *patches*



```
to go
   ask patches
   [
          ; per a cada patch (x,y) calcular  deltap i deltaw
           set deltaw a - ( w * p * p ) + v * ( [w] of patch-at 0 -1 - w )
           set deltap 0 ; completar despres
   ]
   ask patches
   [
          set w  w + deltat * deltaw
          set p  p + deltat * deltap
          if w < 0 [ set w 0 ]
          if p < 0 [ set p 0 ]
   ]
    ask patches
    [
       set pcolor scale-color blue w 0 1
    ]
end
```



Qüestió 1: Implementar el model de "tiger bush".



1) Integrar equacions diferencials (Euler)

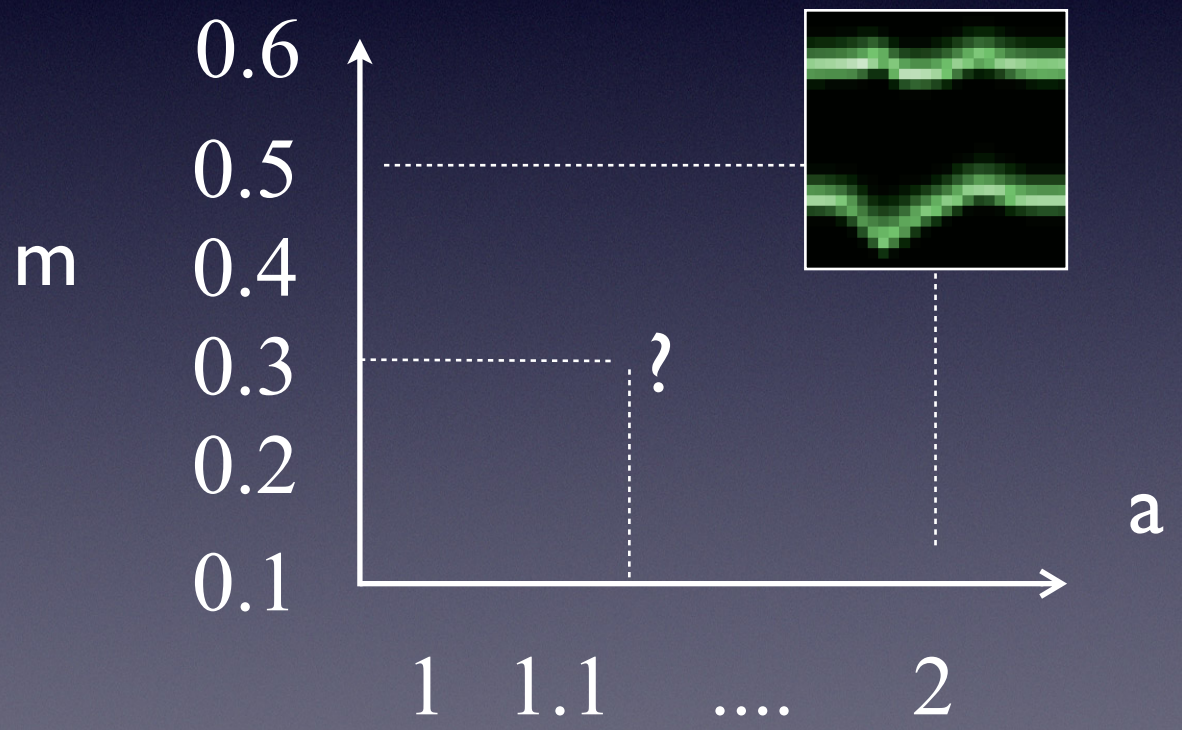
$$\frac{dp}{dt} = wp^2 - mp + D\left(\frac{d^2p}{dx^2} + \frac{d^2p}{dy^2}\right) \longrightarrow \text{deltap}$$

2) Pintar el *patch* de color verd amb escala de colors proporcional a la variable 'p' (`scale-color`)

```
ask patches
[
  set pcolor scale-color green p 0 pmax
]
```

C. A. Klausmeier, “Regular and Irregular Patterns in Semiarid Vegetation” Science 284(5412), pp. 1826–1828 (1999)

Qüestió **3**: Fixat el coeficient de diffusió i explorar l’espai de paràmetres.



OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Agent-Based Model of Therapeutic Adipose-Derived Stromal Cell Trafficking during Ischemia Predicts Ability To Roll on P-Selectin

Alexander M. Bailey[1], Michael B. Lawrence[1], Hulan Shang[2], Adam J. Katz[2], Shayn M. Peirce[1]*

1 Department of Biomedical Engineering, University of Virginia, Charlottesville, Virginia, United States of America, **2** Department of Plastic Surgery, University of Virginia, Charlottesville, Virginia, United States of America

Abstract

Intravenous delivery of human adipose-derived stromal cells (hASCs) is a promising option for the treatment of ischemia. After delivery, hASCs that reside and persist in the injured extravascular space have been shown to aid recovery of tissue perfusion and function, although low rates of incorporation currently limit the safety and efficacy of these therapies. We submit that a better understanding of the trafficking of therapeutic hASCs through the microcirculation is needed to address this and that selective control over their homing (organ- and injury-specific) may be possible by targeting bottlenecks in the homing process. This process, however, is incredibly complex, which merited the use of computational techniques to speed the rate of discovery. We developed a multicell agent-based model (ABM) of hASC trafficking during acute skeletal muscle ischemia, based on over 150 literature-based rules instituted in Netlogo and MatLab software programs. *In silico*, trafficking phenomena within cell populations emerged as a result of the dynamic interactions between adhesion molecule expression, chemokine secretion, integrin affinity states, hemodynamics and microvascular network architectures. As verification, the model reasonably reproduced key aspects of ischemia and trafficking behavior including increases in wall shear stress, upregulation of key cellular adhesion molecules expressed on injured endothelium, increased secretion of inflammatory chemokines and cytokines, quantified levels of monocyte extravasation in selectin knockouts, and circulating monocyte rolling distances. Successful ABM verification prompted us to conduct a series of systematic knockouts *in silico* aimed at identifying the most critical parameters mediating hASC trafficking. Simulations predicted the necessity of an unknown selectin-binding molecule to achieve hASC extravasation, in addition to any rolling behavior mediated by hASC surface expression of CD15s, CD34, CD62e, CD62p, or CD65. *In vitro* experiments confirmed this prediction; a subpopulation of hASCs slowly rolled on immobilized P-selectin at speeds as low as 2 μm/s. Thus, our work led to a fundamentally new understanding of hASC biology, which may have important therapeutic implications.

Citation: Bailey AM, Lawrence MB, Shang H, Katz AJ, Peirce SM (2009) Agent-Based Model of Therapeutic Adipose-Derived Stromal Cell Trafficking during Ischemia Predicts Ability To Roll on P-Selectin. PLoS Comput Biol 5(2): e1000294. doi:10.1371/journal.pcbi.1000294

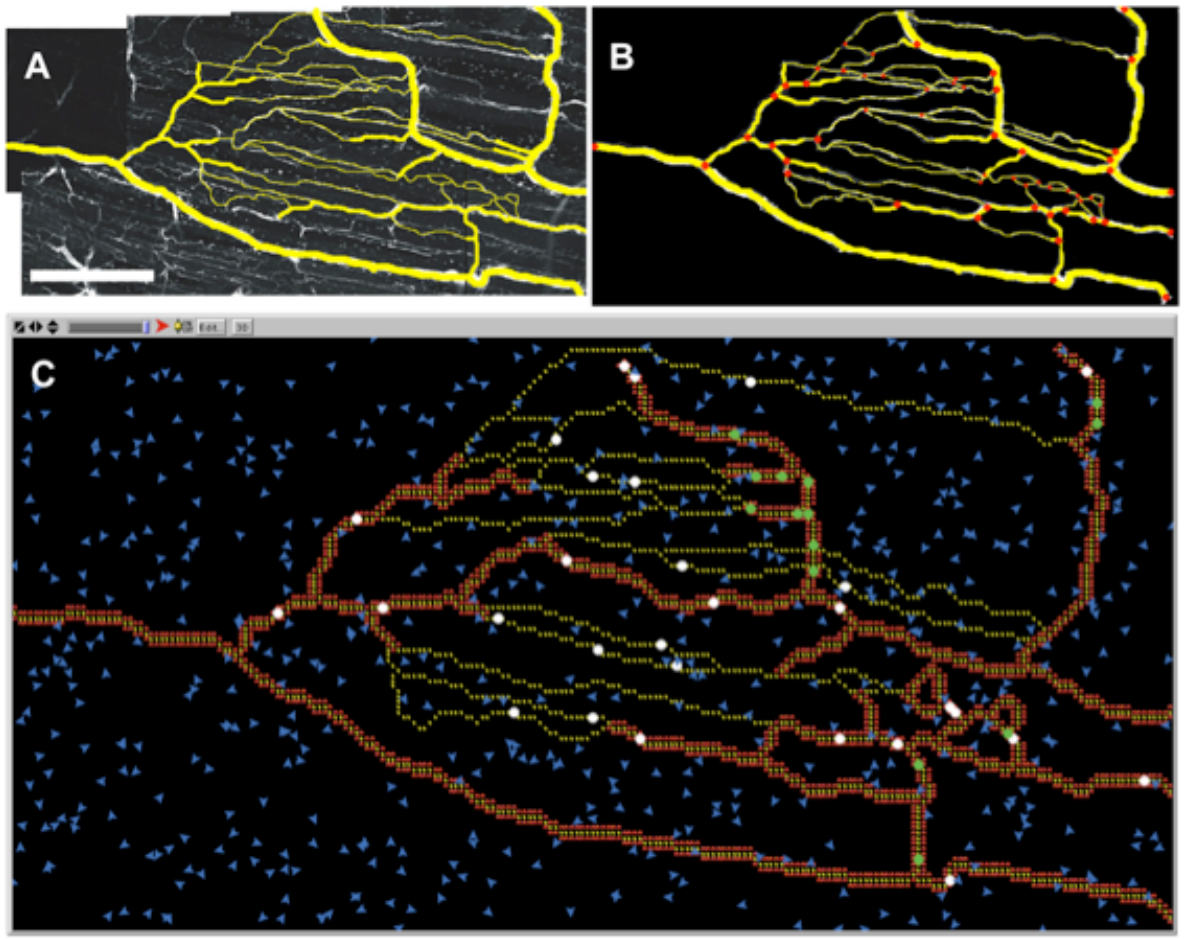
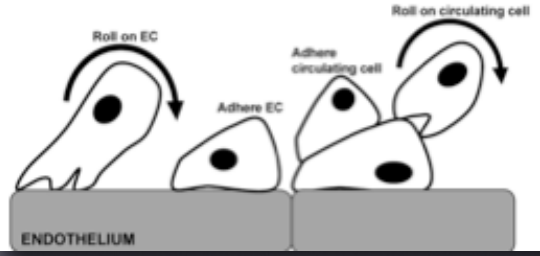


Figure 10. Simulated microvascular network was modeled after mouse skeletal muscle, visualized using confocal microscopy following harvest, using a 20× objective. (A) Confocal microscopy image of mouse spinotrapezius muscle immuno-stained to visualize ECs with BS1-lectin antibody (white). Vascular structures of interest were copied over in yellow in image processing software (ImageJ). Scale bar is 1 mm. (B) The micrograph was manually discretized into nodes, defined as bifurcation points in the microvascular network, and the nodes were connected to form elements. (C) Screen-shot of simulation space. Nodes and elements were manually drawn into the NetLogo simulation space to represent the real microvascular network. Arterioles and venules were characterized on the micrograph based on vessel diameter. Smooth muscle cells are depicted in red lining arterioles and venules. Endothelial cells are depicted in yellow, and tissue macrophages present within the interstitum of the simulation space are depicted in blue.
doi:10.1371/journal.pcbi.1000294.g010



because the focus of this first-generation was on tissue-level changes across entire populations of cells (versus individual cells). During parameterization, however, model outputs were highly sensitive to the frequency of surveying, although relative results remained unchanged (data not shown). To clarify, increasing the survey rate by a factor of ten significantly and substantially increased the degree of both monocyte and hASC extravasation to unrealistic levels, with and without the presence of SBM-X. However, the relative increases in hASC extravasation following the addition of SBM-X in all simulations (low or high survey rate)

Entrega de les pràctiques

Penjar un fitxer .ZIP amb l'informe i el fitxer .nlogo