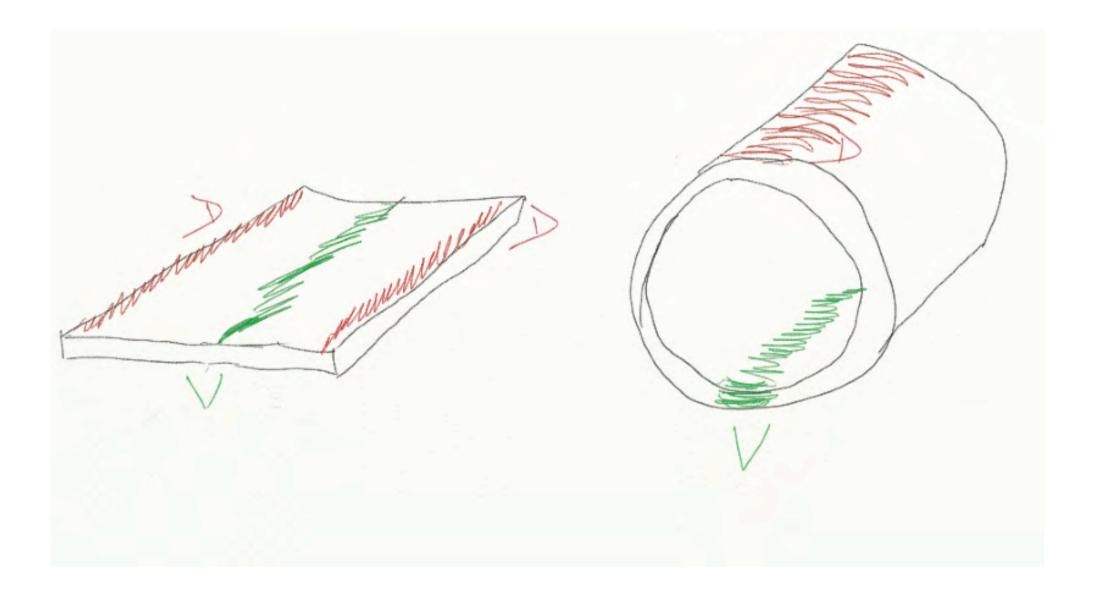
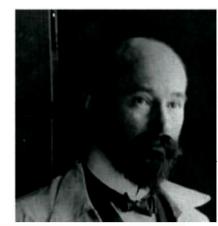
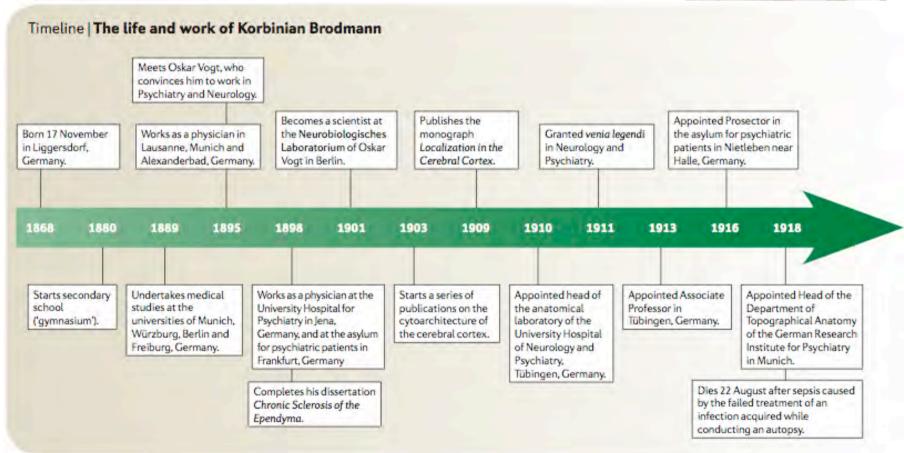
### Cours 3 Octobre 2011

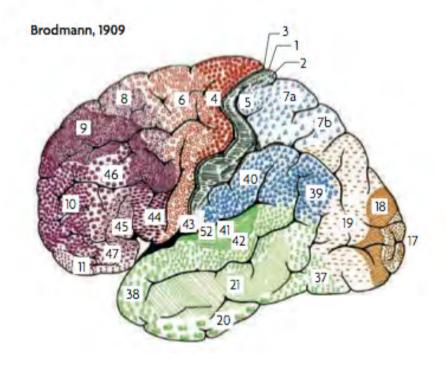


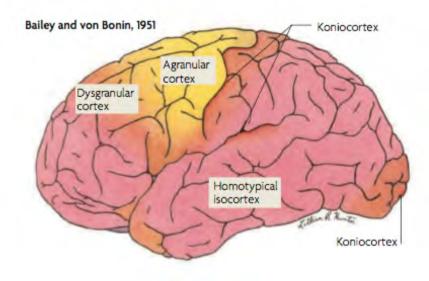
Karl Zilles and Katrin Amunts

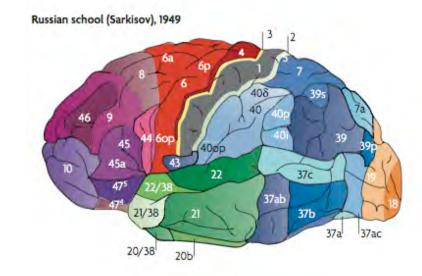




Karl Zilles and Katrin Amunts







#### TIMELINE

### Centenary of Brodmann's map — conception and fate

Karl Zilles and Katrin Amunts

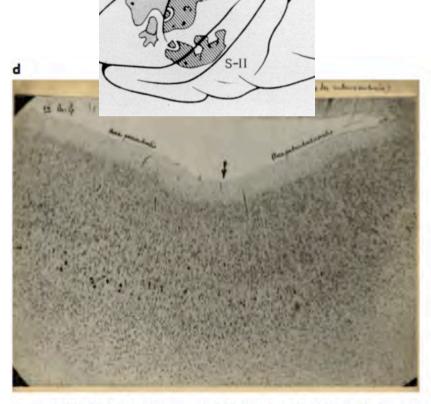
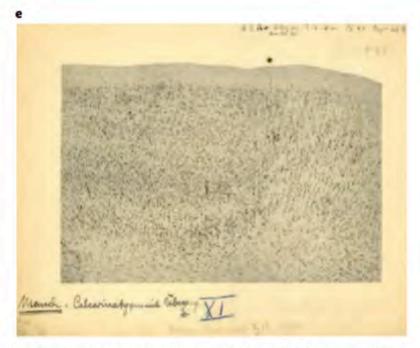


Figure 1 | Korbinian Brodmann and his work. a | Korbinian Brodmann. b | The cover page of Brodmann's seminal monograph from 1909. c | Brodmann in the Neurobiologisches Laboratorium of Cécile and Oskar Vogt in Berlin. d | One of Brodmann's cytoarchitectonic micrographs, showing the border (indicated by the arrow) between Area 4 (primary motor cortex; left side) and Area 3 (primary somatosensory cortex; right side). The handwritten inscription in the upper right corner reads (in translation):



"transition between type 4 and type 3; anterior wall of the central sulcus".

e | Another of Brodmann's cytoarchitectonic maps, showing the border (indicated by the asterisk) between area 17 (primary visual cortex (V1)) and area 18 (secondary visual cortex (V2)). The handwritten inscription in the lower left corner reads (in translation): "human brain: calcarina type with transition". The images are reproduced, with permission, from the archive of the C. & O. Vogt-Institute of Brain Research, University Düsseldorf, Germany.

Karl Zilles and Katrin Amunts

#### Autoradiography muscarinic receptor M2

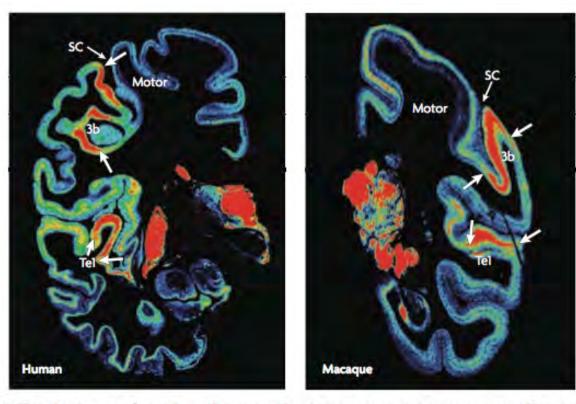
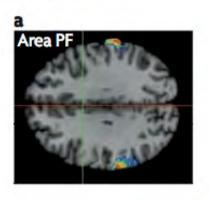
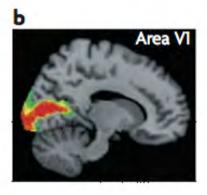


Figure 4 | Cortical maps based on the quantitative in vitro receptor autoradiography of the regional and laminar distribution of neurotransmitter receptors in the human and macaque brain. a | Cholinergic muscarinic M2 receptors (labelled with [3H]oxotremorine-M) in coronal sections through a human (left) and a macaque (right) hemisphere. Homologous cortical areas show identical (for example, 3b primary somatosensory cortex, Te1 (REF. 44), primary auditory cortex) or very similar (for example, motor cortex) regional and laminar expression levels of this muscarinic subtype. b | Various transmitter receptors around the central sulcus demonstrate the segregation

Karl Zilles and Katrin Amunts





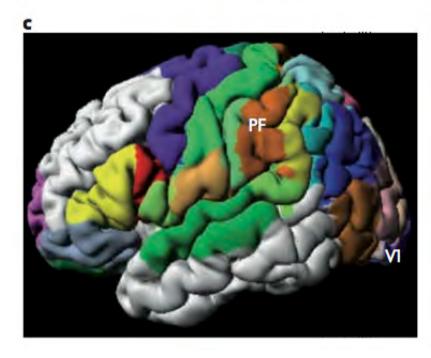
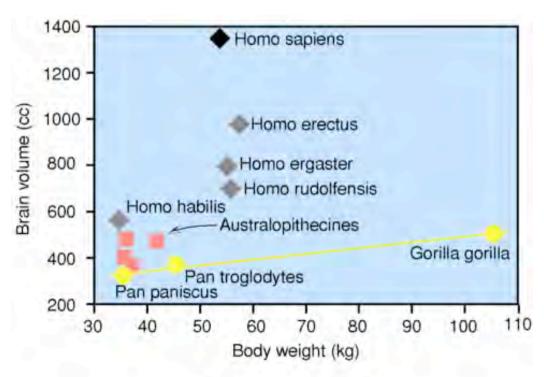


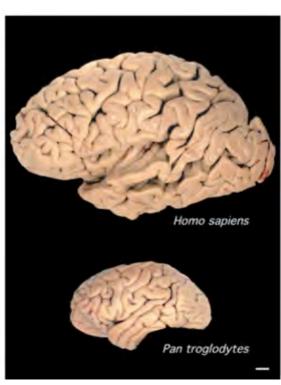
Figure 3 | Probability maps of the human cortex based on quantitative cytoarchitecture and statistical tests for the localization of borders between areas. The Jülich-Düsseldorf cytoarchitectonic probabilistic brain atlas is based on observer-independent mapping of cortical areas in ten post-mortem brains<sup>34,41</sup>. a,b | Cytoarchitectonic probabilistic maps of (a) area PF of the inferior parietal lobule (corresponding to a part of Brodmann's area 40) and (b) the primary visual area (V1) (corresponding to Brodmann's area 17) in standard reference space of the MNI42,43. Red indicates regions of high overlap (low intersubject variability); blue-green indicates regions of low overlap (high variability). c | Lateral view of the MNI reference brain with maximum probability map, illustrating the current status of the lülich-Düsseldorf atlas. The maximum probability map<sup>30</sup> has been generated on the basis of cytoarchitectonic probabilistic maps in standard reference space; it assigns each voxel of the reference space to the area with the highest probability. Grey regions are not yet mapped. Published maps are available at: http://www.fzjuelich.de/inm/spm\_anatomy\_toolbox. Part b is modified, with permission, from REF. 32 @ (2006) Macmillan Publishers Ltd. All rights reserved.

### Human c Human 37 Lemur **b** Macaque 19 .18 10 & 11 13-16 a Mouse 51 20 28

#### **HOMINIDÉS**

		Cerveau (cm3)	Taille (m)
Australopithèques	-2,5/-0,750 (Lucy)	300-400	1,10
Homo habilis (outils)	-1,8M/-0,750M	600-700	1,30-1,50
Homo erectus	-1,2M/-0,120M	800-1000	1,50-1,70
Anténéandertaliens (feu)	-0,750/-0,100M	1100-1400	1,60-1,70
Néandertaliens (sépultures)	-0,120/-0,035M	1200-1740	1,65-1,70
Homo sapiens (art)	-0,120M	1450-1650	1,60-1,80





#### COMPARTMENTS AND THEIR BOUNDARIES IN VERTEBRATE BRAIN DEVELOPMENT

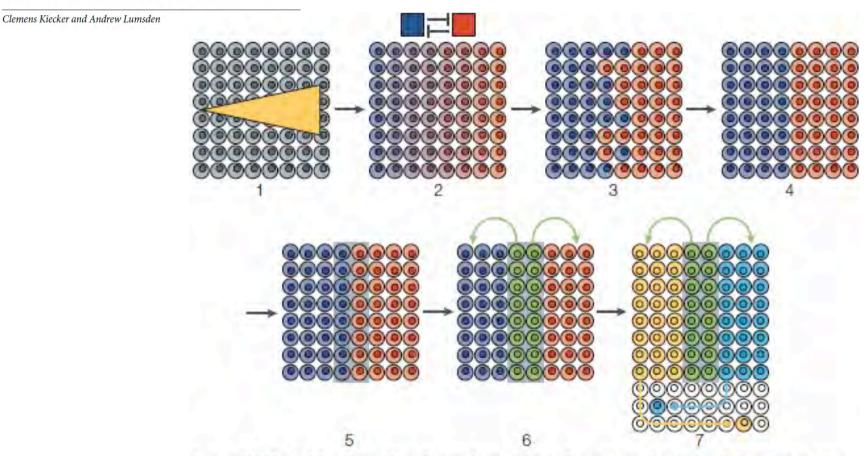


Figure 6 | Model for boundary formation. An initially uniform sheet of cells is polarized by an early signalling gradient (yellow; 1), which results in a coarse prepattern of transcription factor expression (red/blue; 2). Mutual repressive interactions between these factors establish two distinct populations of cells that are separated by a fuzzy interface (3). Cell-sorting processes result in a sharpening of this interface (4), and a specific boundary phenotype (loss of adhesion, expression of specific boundary markers) is generated (shaded area; 5). The boundary cells express signalling factors (green; 6) that induce prepattern-dependent cell fates (yellow/turquoise) in the adjacent territories. Postmitotic cells might be able to cross the boundary, as their fates are sealed (7).

# One hundred years of positional information

LEWIS WOLPERT

TIG SEPTEMBER 1996 VOL. 12 No. 9

168-9525/95/515 00

359

One mechanism by which spatial patterns of cell differentiation could be specified during embryonic development and regeneration is based on positional information. Cells acquire a positional value with respect to boundaries and then interpret this in terms of a programme determined by their genetic constitution and developmental history. The signals and the molecular basis of such a system have both been rather well conserved. Recent work has shown that cells can respond to quite small differences in the concentrations of molecules whose concentration could broated positional information.

With respect to boundaries

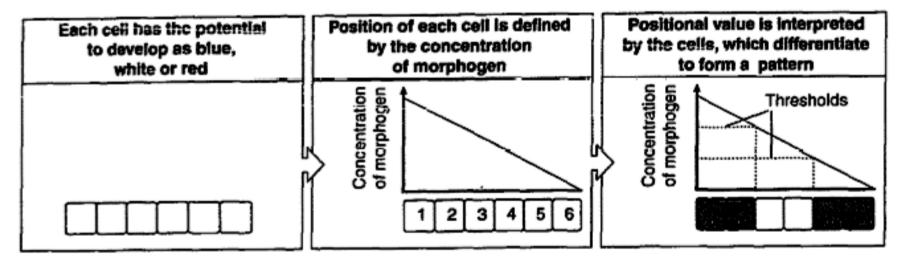


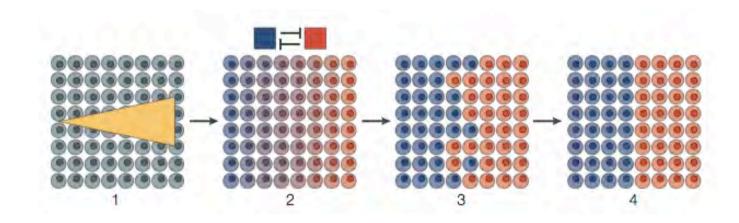
FIGURE 1. The French flag model for thinking about pattern formation. The cells in a line can differentiate as blue, white or red. They can be programmed to make a French flag pattern if they have their position specified and interpret this infomation. One mechanism can use a morphogen gradient and thresholds. The boundary values are crucial and the slope of the gradient gives the system its polarity. (Reproduced, with permission, from Ref. 26.)

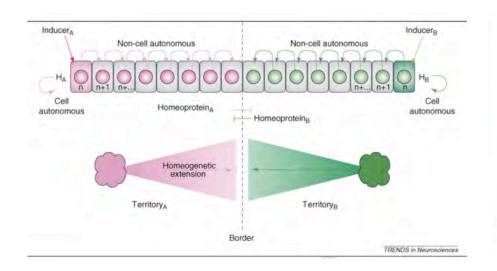
#### Messenger proteins or "diffusible genes" or morphogens?

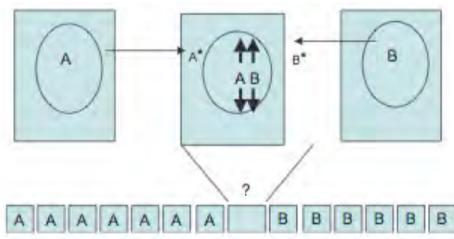
The substances will be called morphogens, the word being intended to convey the idea of a form producer. It is not intended to have any very exact meaning, but is simply the kind of substance concerned in this theory. The evocators of Waddington provide a good example of morphogens (Waddington 1940). These evocators diffusing into a tissue somehow persuade it to develop along different lines from those which would have been followed in its absence. The genes themselves may also be considered to be morphogens. But they form rather a special class. They are quite indiffusible. Moreover; it is only by courtesy that genes can be regarded as separate molecules. It would be more accurate (at any rate at mitosis) to regard them as radicals of the giant molecules known as chromosomes. But presumably these radicals act almost independently, so that it is unlikely that serious errors will arise through regarding the genes as molecules...

Alan M. Turing, The chemical basis of morphogenesis, 1952

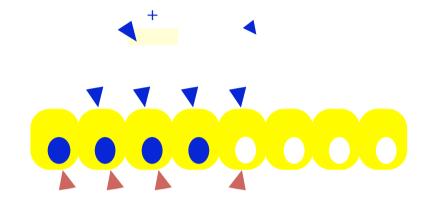
#### **Gradients and Boundaries**



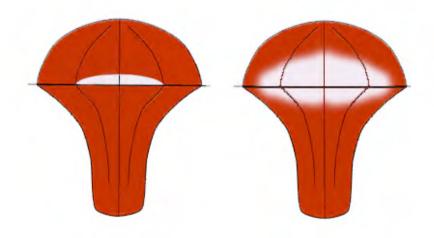




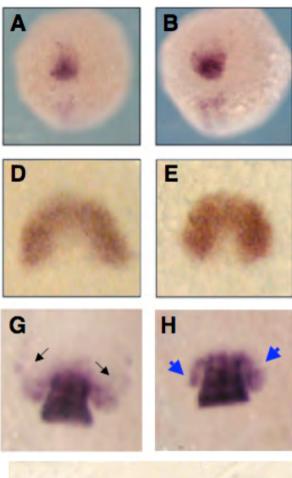
### INDUCTION AND HOMEOGENETIC EXTENSION

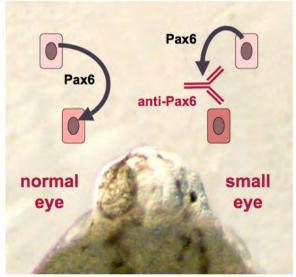


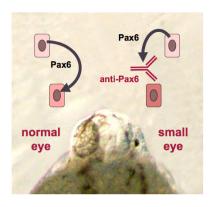
Planar

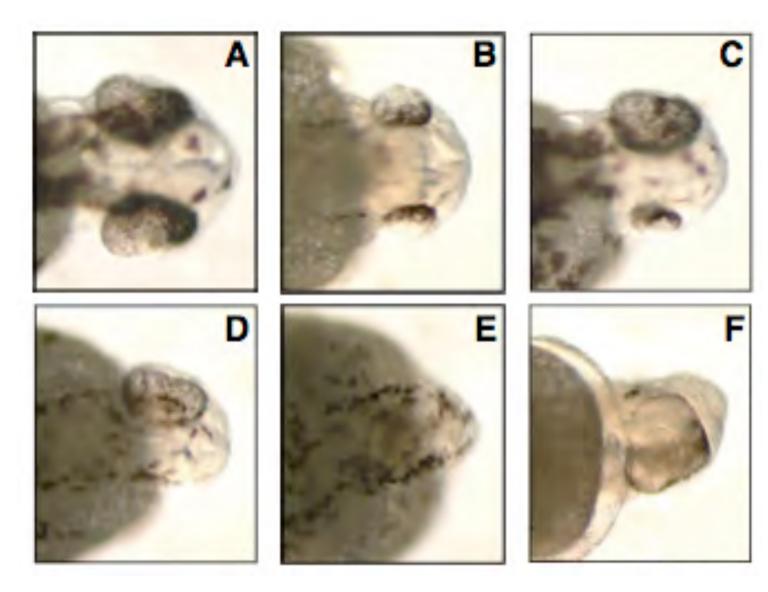


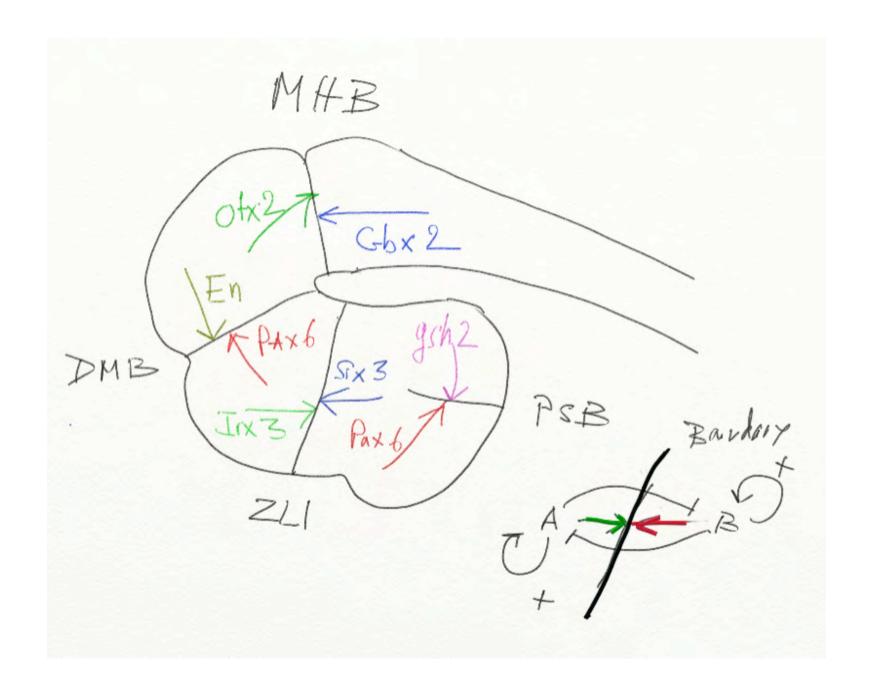
Lesaffre et al., Neural dev. 2007







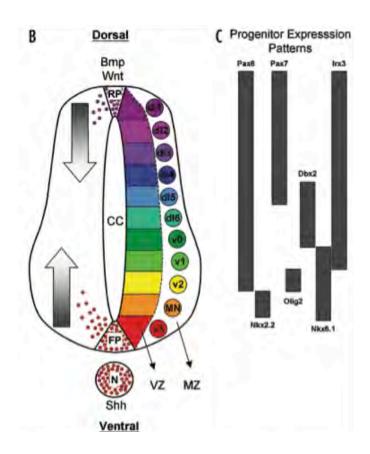


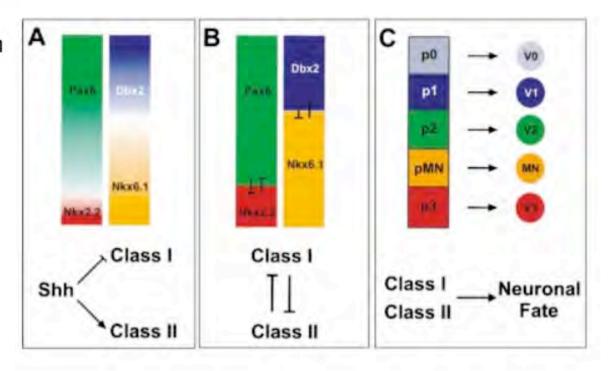


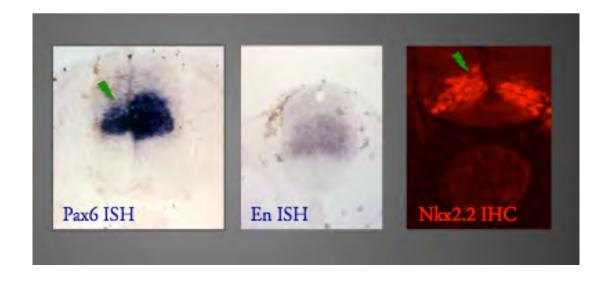
#### Review

### Morphogens and the Control of Cell Proliferation and Patterning in the Spinal Cord

Fausto Ulloa<sup>1</sup> James Briscoe<sup>2</sup>



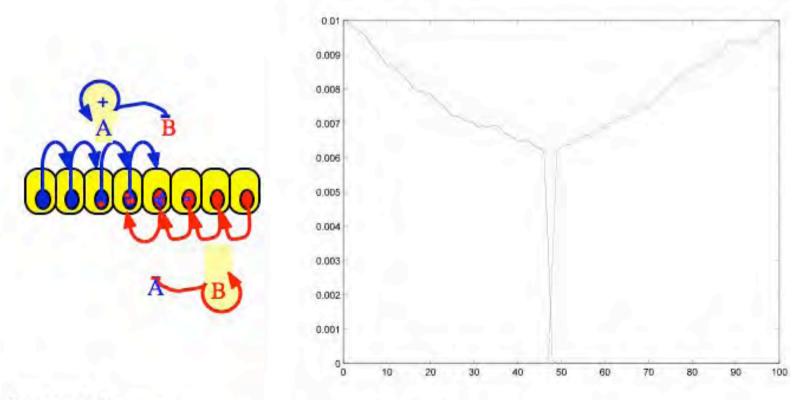




#### Modeling homeoprotein intercellular transfer unveils a parsimonious mechanism for gradient and boundary formation in early brain development

D. Holcman a,b,\*,1, V. Kasatkina, A. Prochiantzc

## Effect of random fluctuations on the position of the boundary



Stochastic flux

Cumulative effect of a flux of 1% at each cell=shift of a 2 to 3 cells

#### Modeling homeoprotein intercellular transfer unveils a parsimonious mechanism for gradient and boundary formation in early brain development

D. Holcman a,b,\*,1, V. Kasatkina, A. Prochiantzc

