Computational models for understanding development of retinotopic maps

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Background

Slides

Available at: `http://bit.ly/eglen-nijmegen`

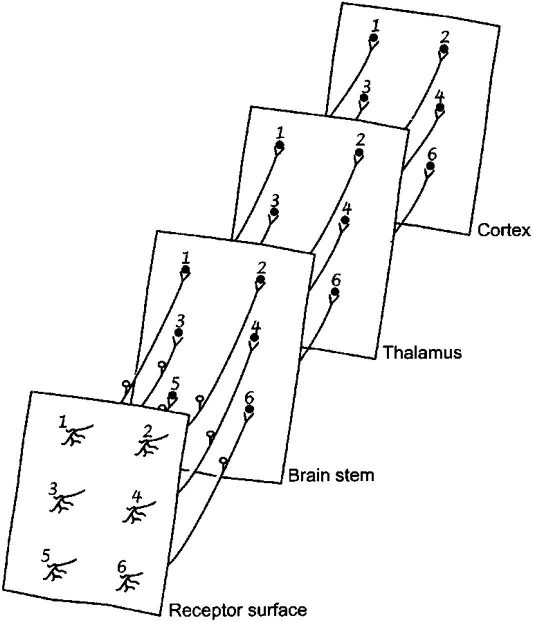
References

Available at: `http://bit.ly/eglen-n-refs`

Acknowledgements

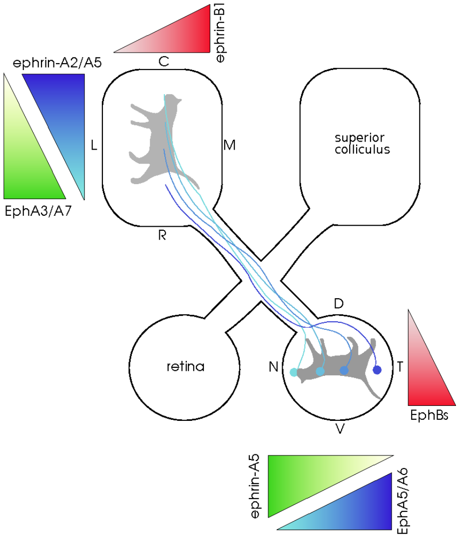
Catherine Cutts, Johannes Hjorth, David Sterratt, David Willshaw. Paperpile.

What is a topographic map?



(Kaas, 2002)

What is a retinotopic map?

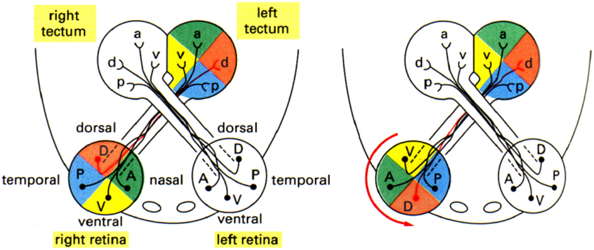


Sperry’s experiments

Sperry’s experiments:

1) Rotation of the eyes of a newt or frog by 180°.
2) Cutting of the optic nerves prior to rotation of the eyes by 180°.

In both experiments the animals see their world upside down and back to front. This condition is irreversible.



Result of rotation

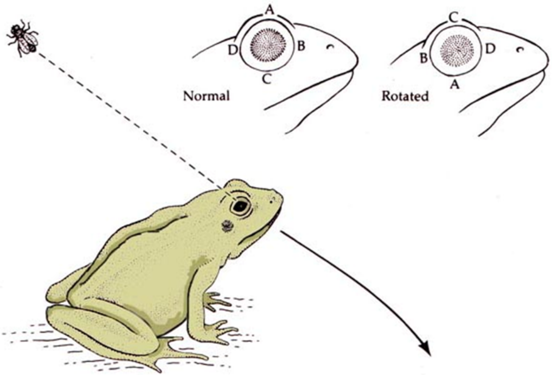
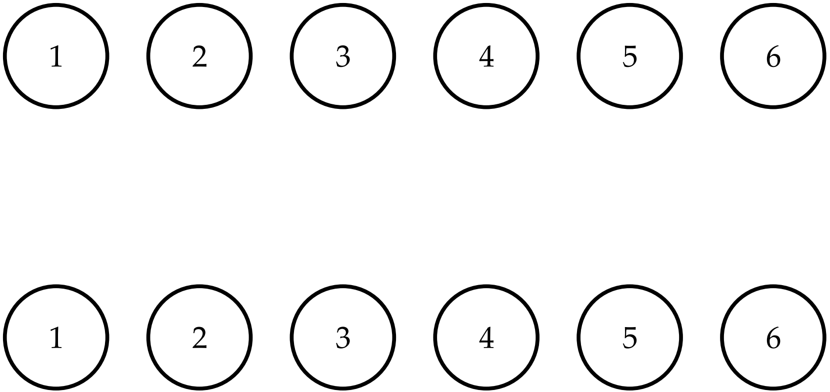
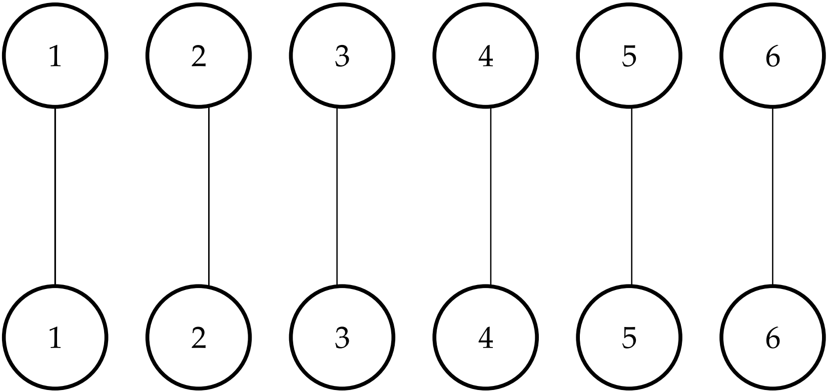


Fig. 21. When the eye is rotated 180¡, the frog's prey catching behavior is inverted. (after Sperry, 1956).

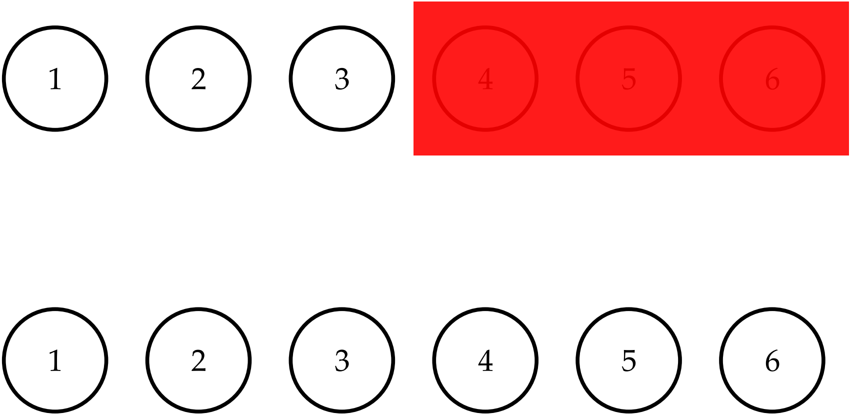
The concept of labels



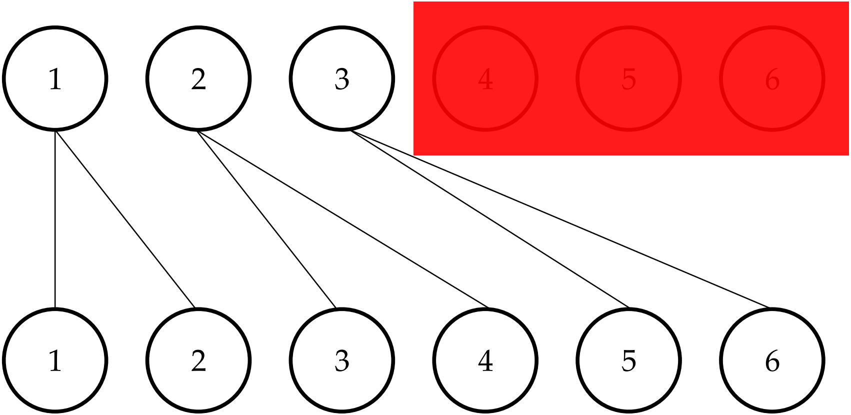
The concept of labels



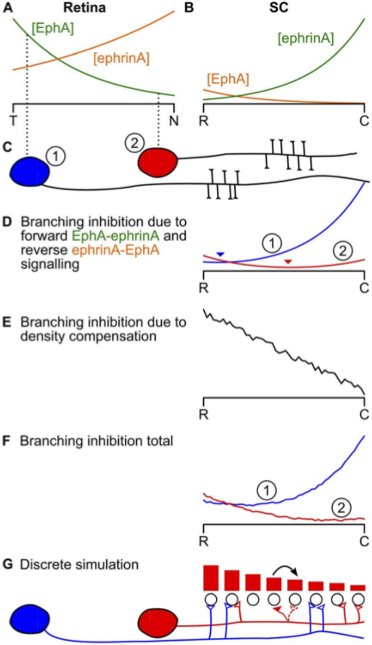
The concept of labels



The concept of labels



Energy-model for branching (Gierer 1983; Sterratt 2013).



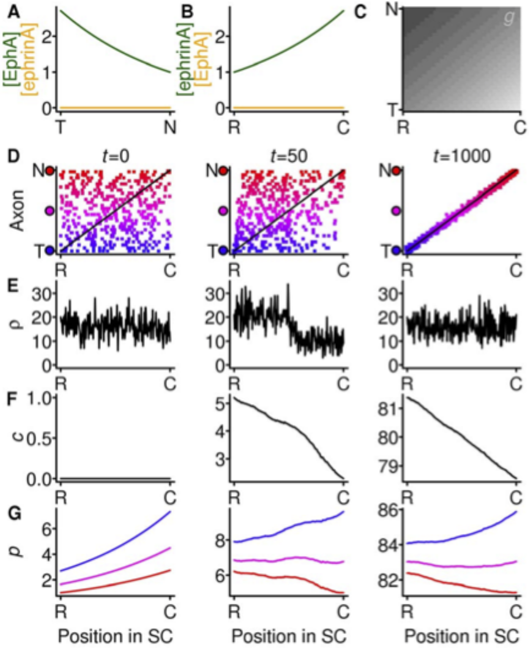
$$g(x,u,t) = [EphA](u)[ephrinA](x) + ephrinA^*(u)[EphA^*](x)$$

$$\frac{\mathrm{d}c}{\mathrm{d}t} = \epsilon p(x,t) - \eta c(x,t)$$

$$p(x,u,t) = g(x,u,t) + c(x,t)$$

(Sterratt 2013)

Wild-type development: 1D



(Sterratt 2013)

Seeing 2d maps

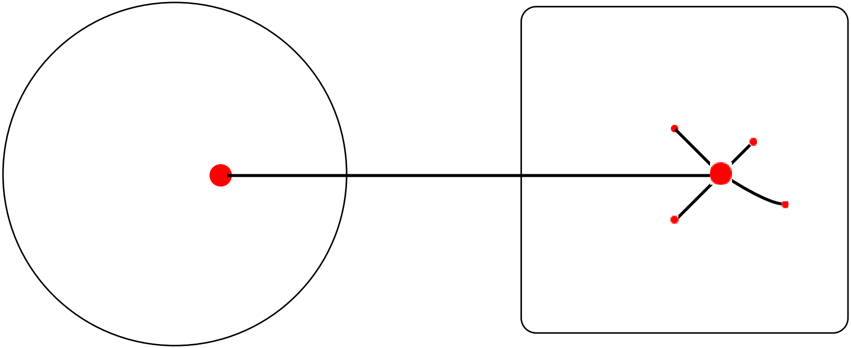


Figure 1: One RGC into target

Seeing 2d maps

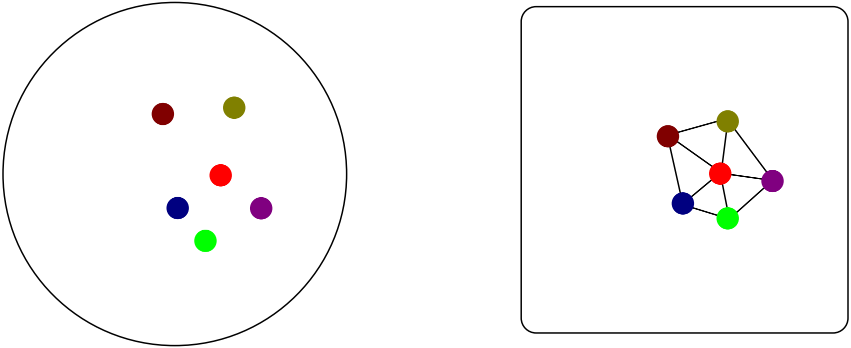
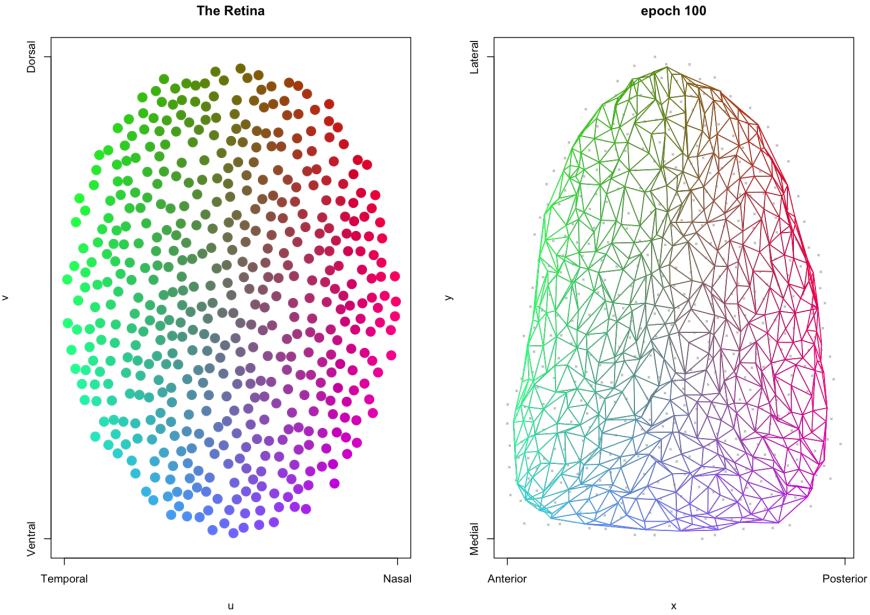
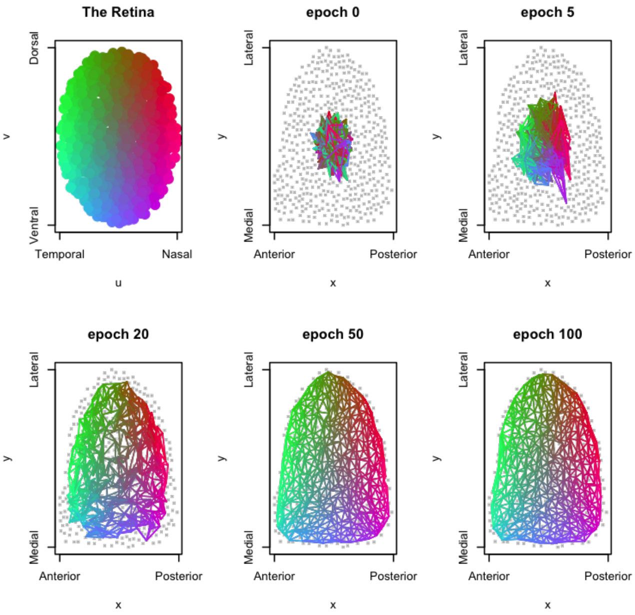


Figure 1: Mesh generated

2D Wild type: final map



2D Wild type: development



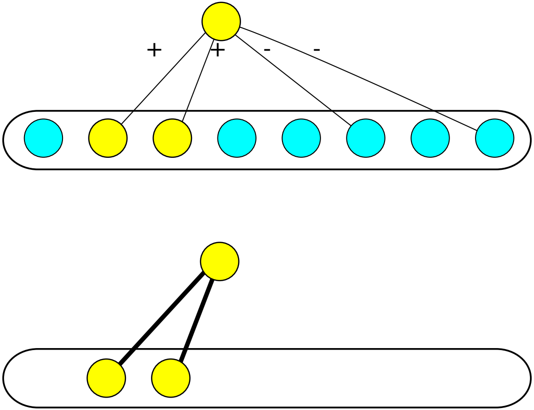
Principles of topographic map formation

Key elements of map formation, demonstrated by Willshaw & von der Malsburg (1976):

1. Neighbouring presynaptic neurons fire in synchrony (retinal waves).
2. Cells that fire together wire together.
3. Neighbouring postsynaptic neurons should develop similar connections.
4. Constraints on synaptic growth (normalisation).
5. Map polarity.

1. Activity as a cue for neighbours

Cells that are neighbours in retina could fire together to show their similarity. Before discovery of retinal waves.

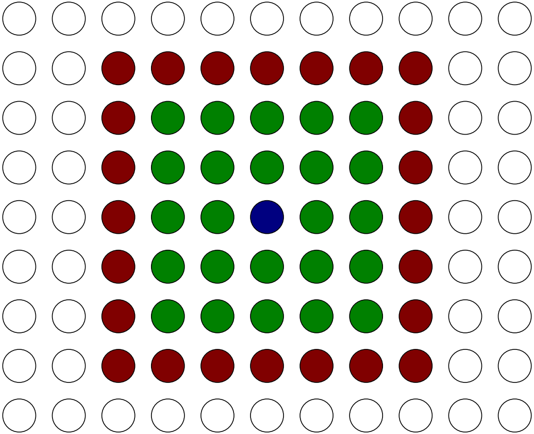


2. Cells that fire together wire together

Output is a weighted function of input activity.

3. Correlated output

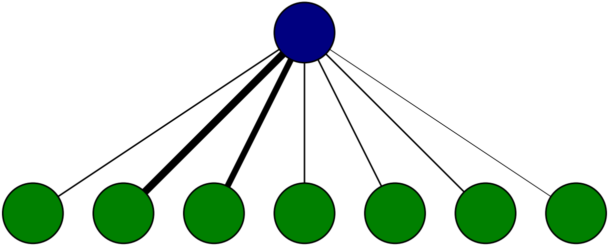
Short-range excitatory (green); longer-range inhibitory (red). Additional growth rules.



4. Normalisation

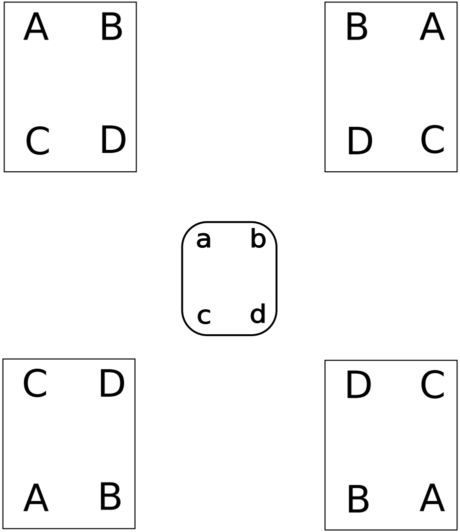
Sum of weights synapsing onto one target neuron (j, blue) is constant.

$$\sum_i w_{ij} = K$$

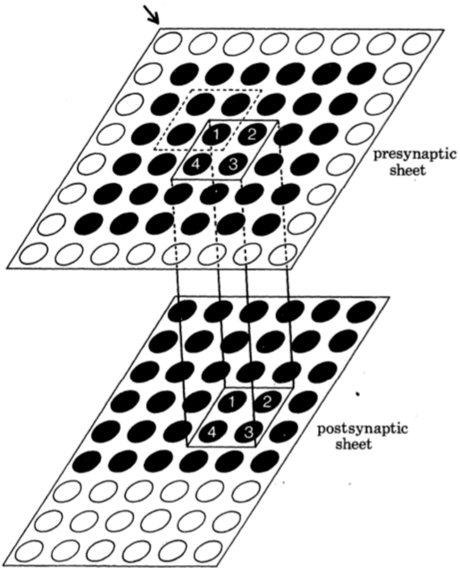


5. The problem of map polarity

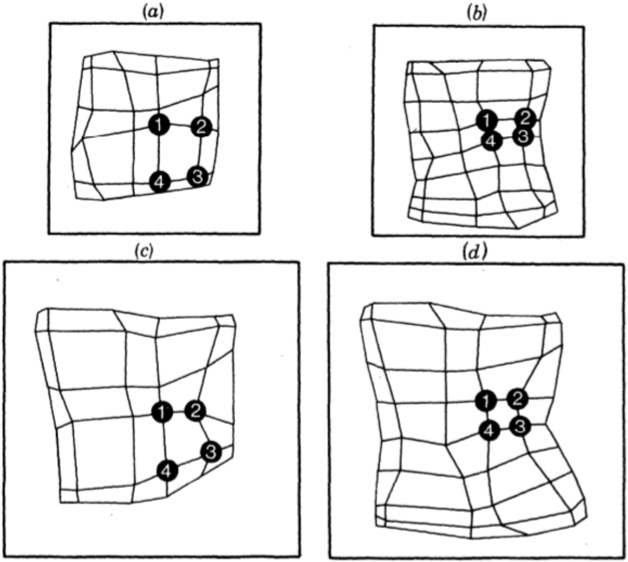
How many ways are there to map one rectangle onto another?



5. Polarity markers in the model



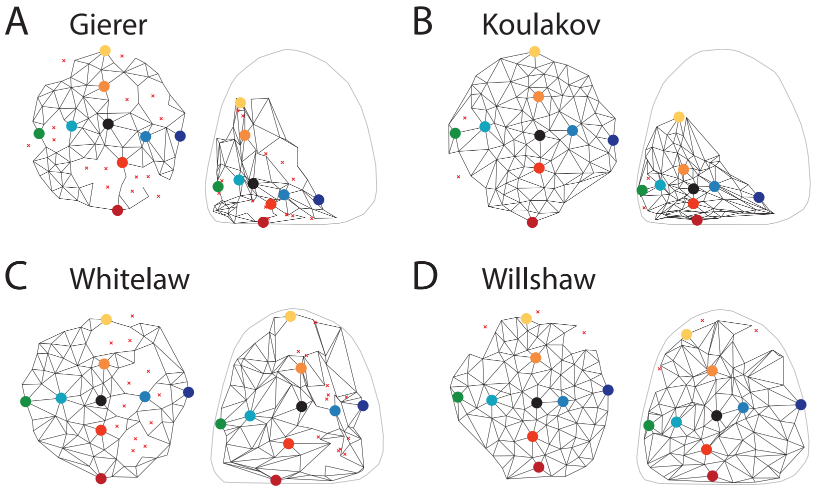
Results: systems matching



Fourty years, fourty models…

Which model is best?

Math5 mutant mouse



Competition framework to test models

Genotype	Gierer	Koulakov	Whitelaw	Willshaw
Wild type	✓	✓	✓	* ✓
Isl2-EphA3$^{\mathrm{ki/ki}}$	Isl2^{+} misfit	Isl2^{+} misfit	* ✓	Isl2^{+} misfit
Isl2-EphA3$^{\mathrm{ki/+}}$	No collapse, Isl2^{+} misfit	* Isl2^{+} misfit	No collapse, Isl2^{+} misfit	No collapse, Isl2^{+} misfit
TKO (no gradient)	No patches	Patches but no global order	No patches	Global order but no polarity
TKO (weak gradient)	No patches	✓	No patches	Ordered map
Math5$^{-/-}$	* ✓	✓	Normal map	Normal map

Asterisk (*) denotes which phenotype the model was optimized for.

(Hjorth et al., 2013)

Future directions

1. Matching development of maps
2. Alignment of maps
3. Accounting for all mutants
4. Species-specific differences

Computational resources

Our competition framework

`https://github.com/Hjorthmedh/RetinalMap`
Pipeline for model evaluation.

Topographica

`https://ioam.github.io/topographica/`
General tool (python/gui) for making topographic maps (ocular dominance, orientation selectivity)