GDR BioComp October 2015

Variability and probability in Living Organisms

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Deep Blue beats Garry Kasparov (1997)

LOGIC WORLD ≠ REAL WORLD

Computers outperform human in all logical & arithmetic operations.

Living organisms outperform computers and robots in all tasks involving uncertainty, e.g. action & perception in the real world.

A difference exploited in the « captcha » tests.

OVERVIEW

1. The one-to-many problem

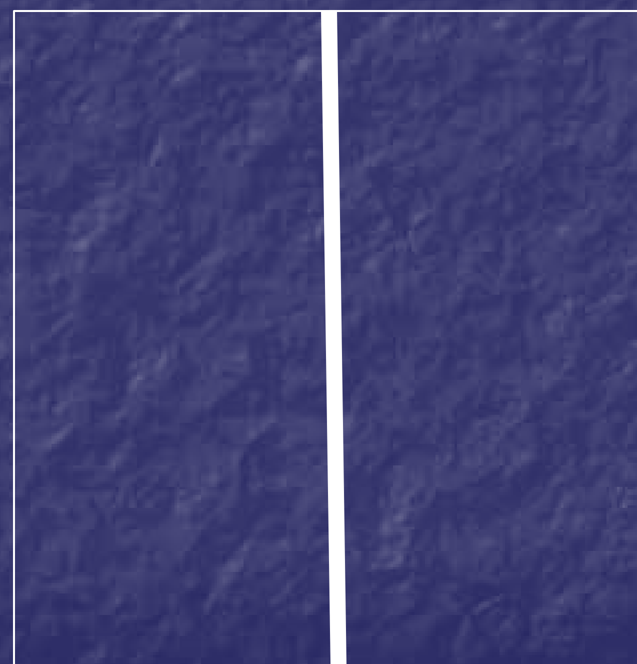
2. The Bayesian Brain

3. The Bayesian Cell

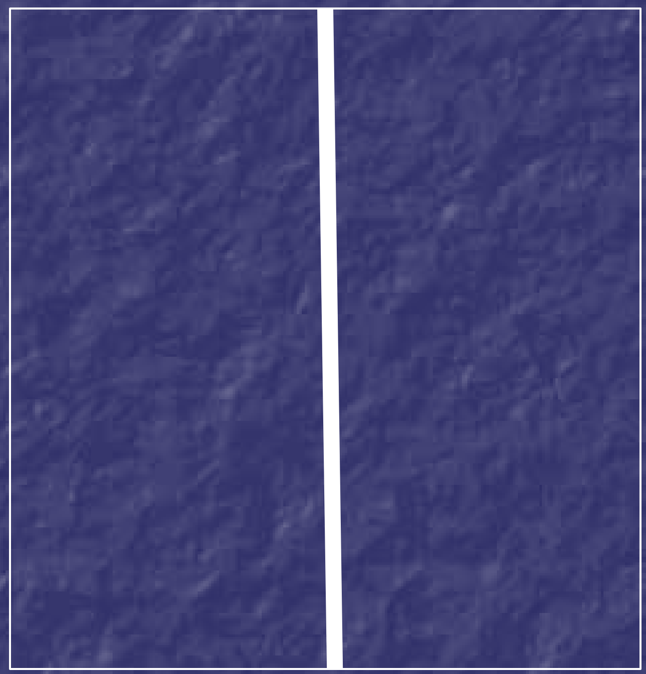
The One-to-Many Problem

Perception as an inference problem: an old idea

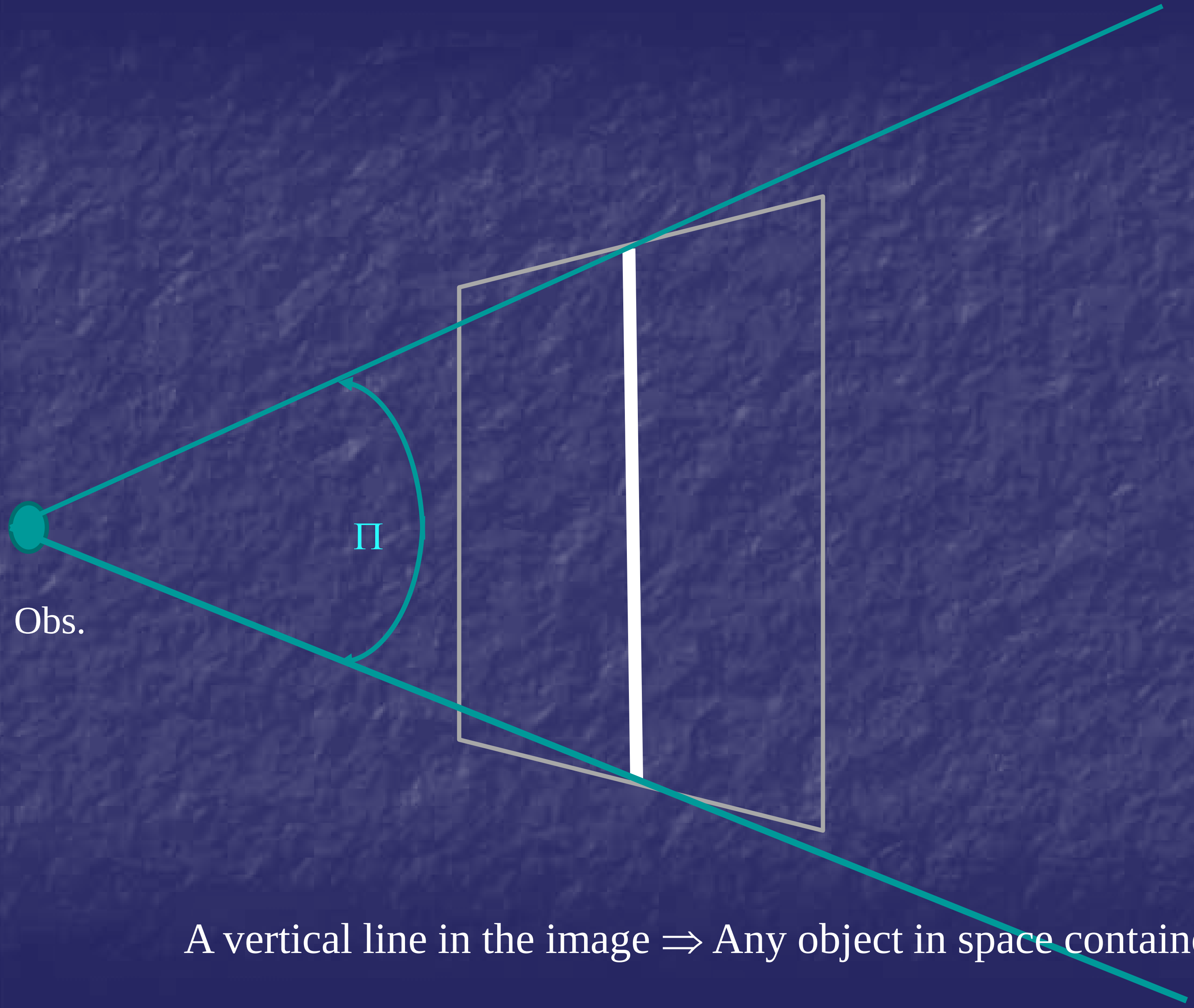
H. Helmholtz (1867), E. Mach (1897), …
Knill & Richards (1996), Kersten, Mamassian & Yuille (2004), …



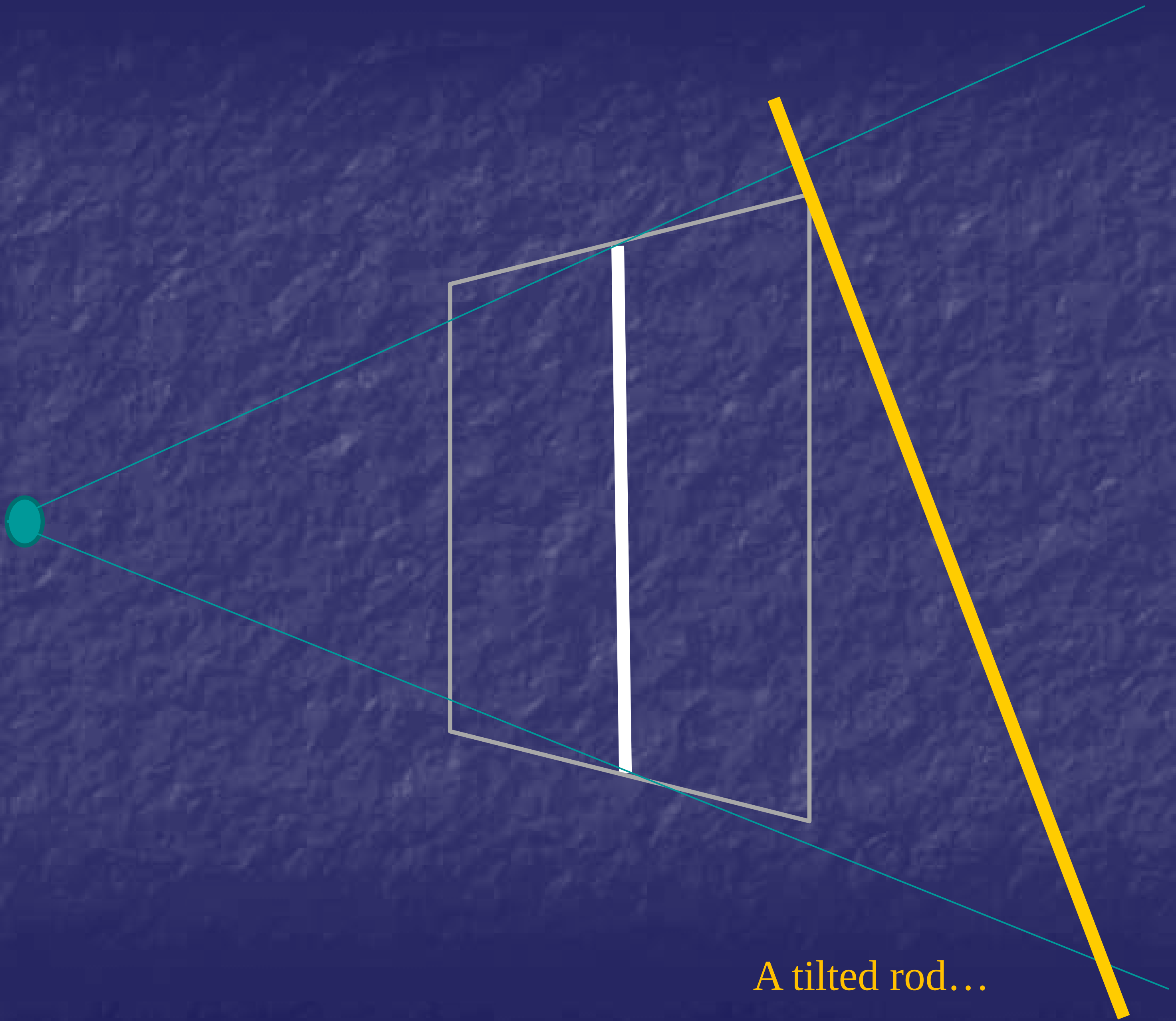
Here, an example from Ernst Mach, *The Analysis of Sensations* (1897)



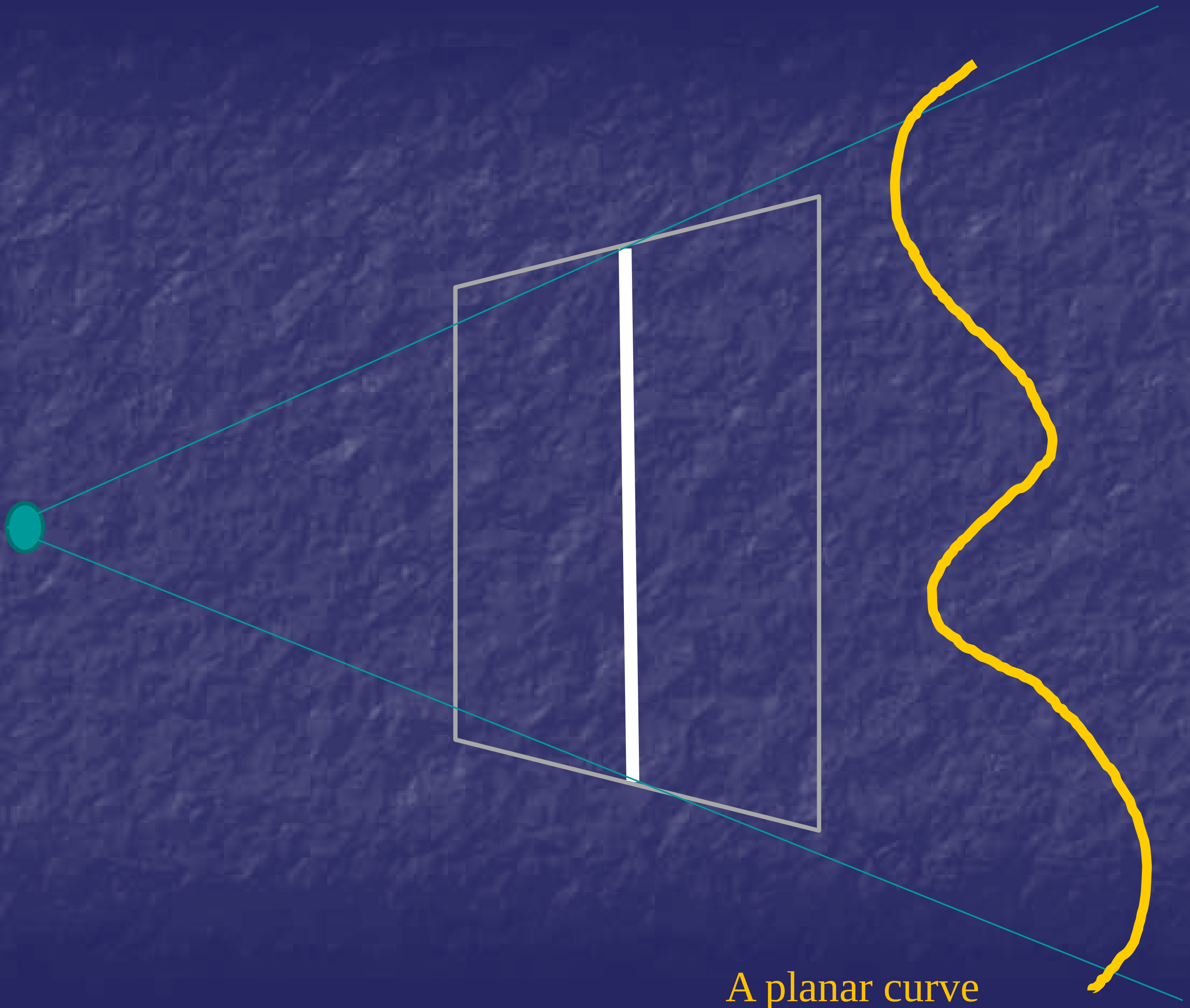
A vertical line in the image ⇒ A vertical rod in space ?



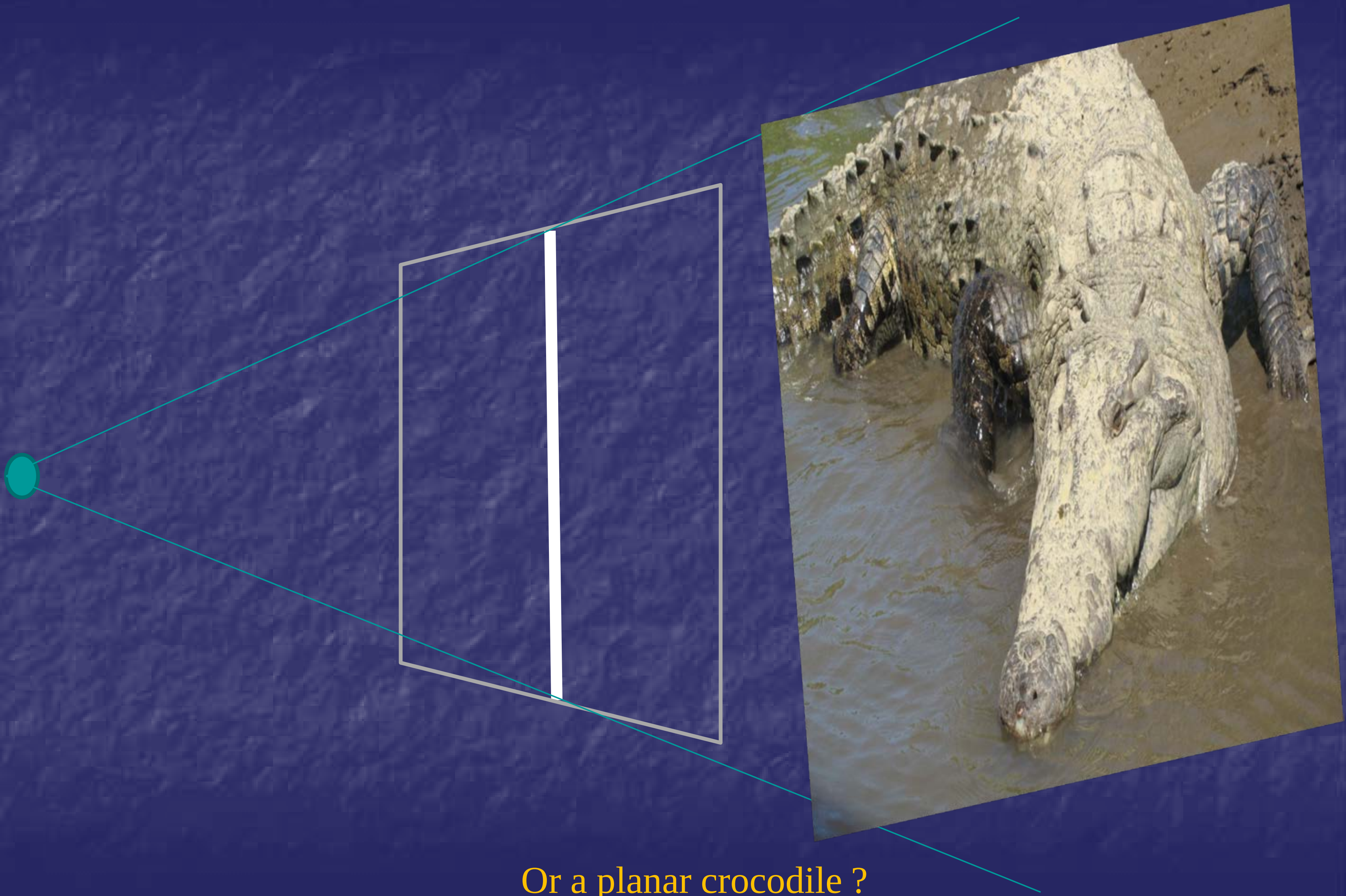
A vertical line in the image ⇒ Any object in space contained in the plane Π



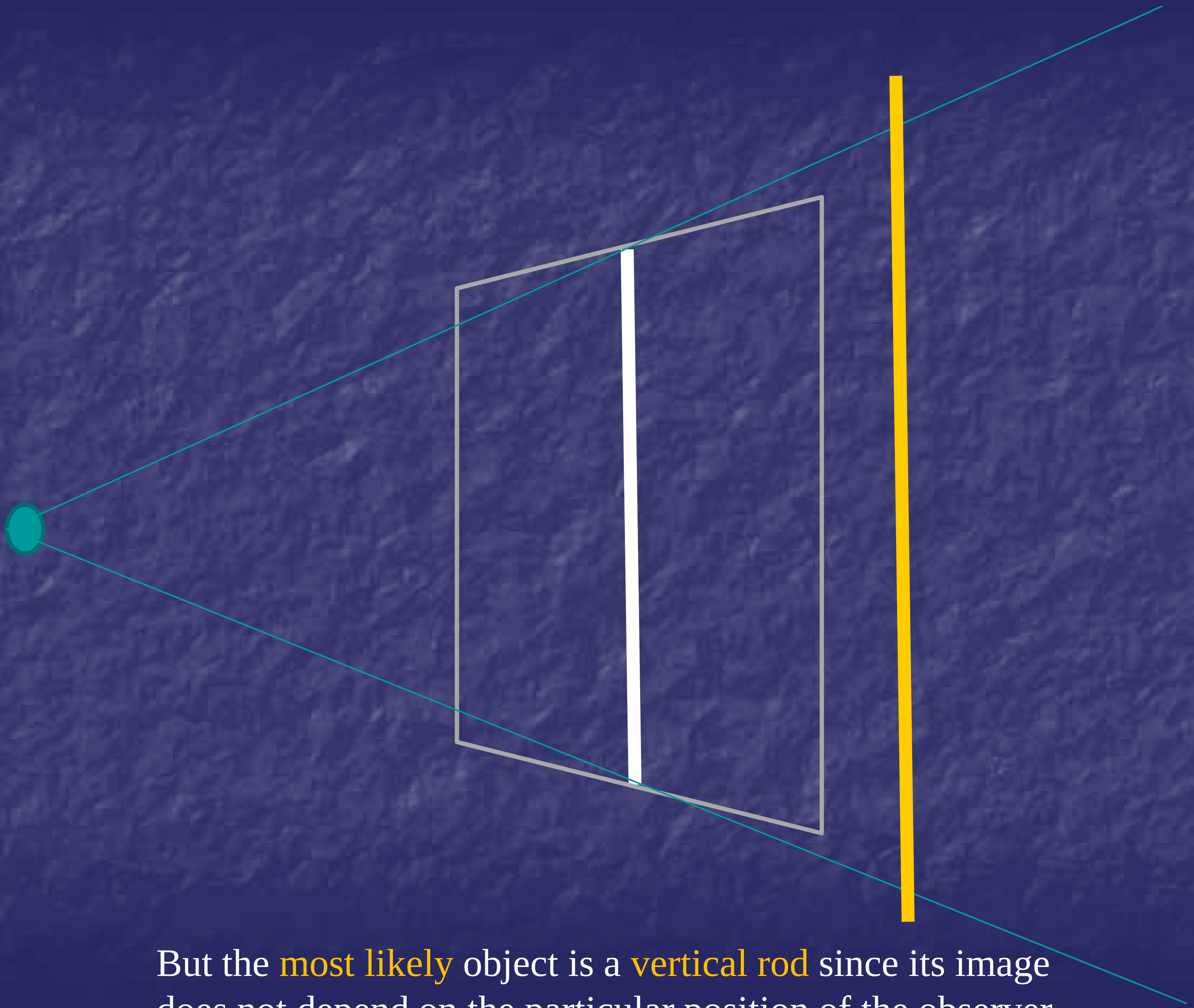
A tilted rod…



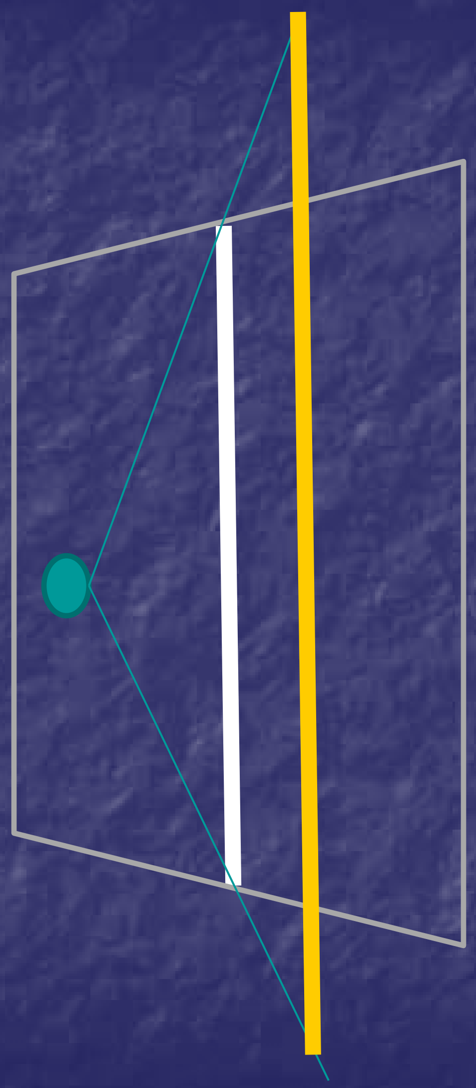
A planar curve



Or a planar crocodile ?

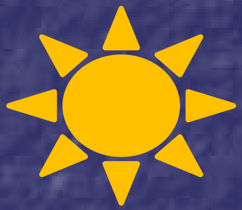


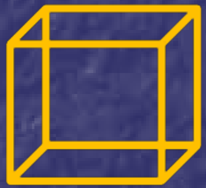
But the most likely object is a vertical rod since its image does not depend on the particular position of the observer.



High P(Image | Object): We do not believe in coincidences !

The Bayesian approach: priors, likelihood and free variables





Perceived Object or State S

Light source F

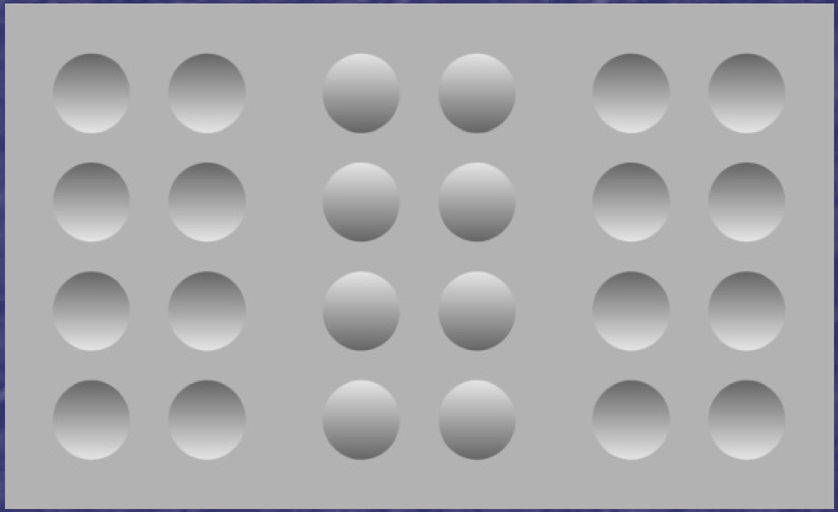
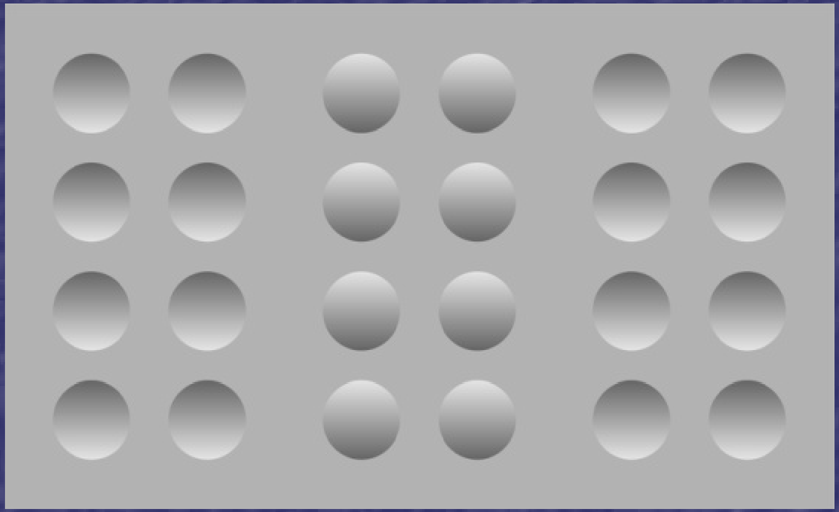
Sensory Observation O

Priors $P(S)$, $P(F)$
(symmetry, regularity, …)

Likelihood $P(O \mid S, F)$
(The sensor function)

Posterior $P(S \mid O) \propto P(S)\, \Sigma_F\, P(F).P(O \mid S, F)$
(Bayes' rule, marginalization rule and normalization)

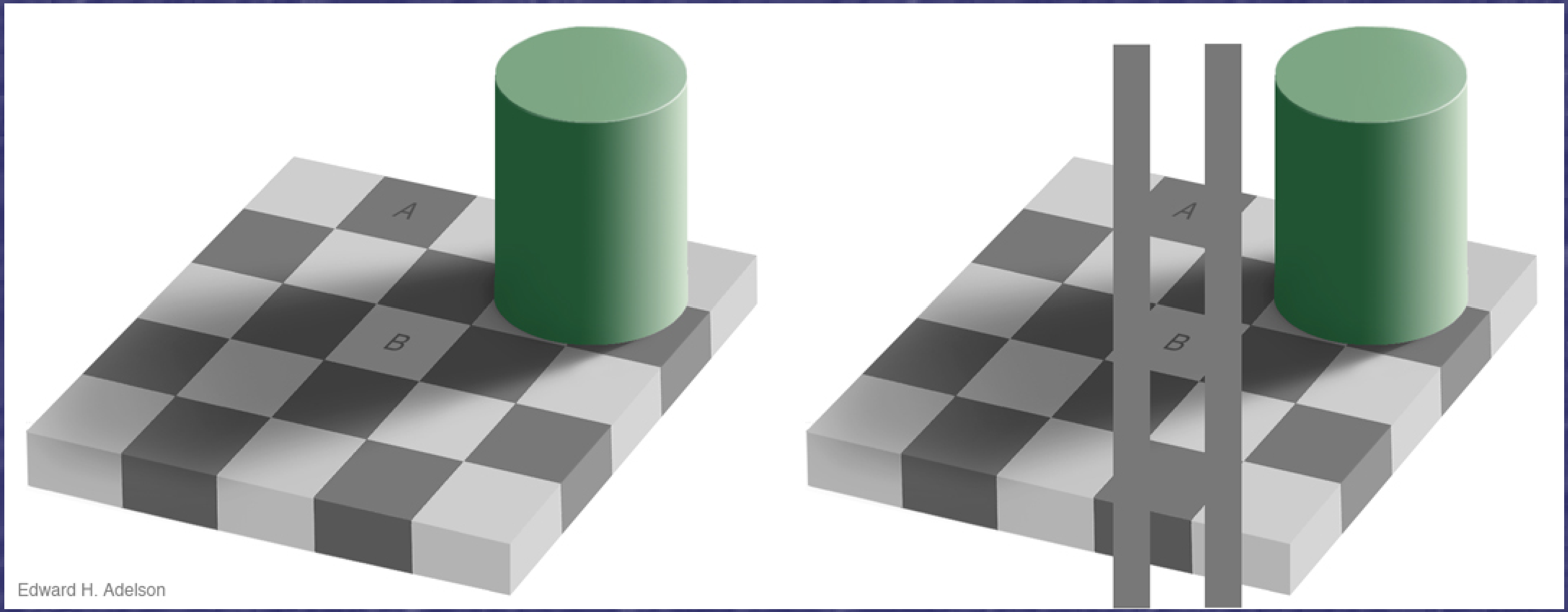
3D Shape from shadow

A priori, the light comes from above (The sun !): the shading is interpreted as « hollows » (if the dark part is above) or « bumps » (if the dark part is below).

Mamassian & Goutcher (2001) Prior knowledge on the illumination position. Cognition 81: B1-9

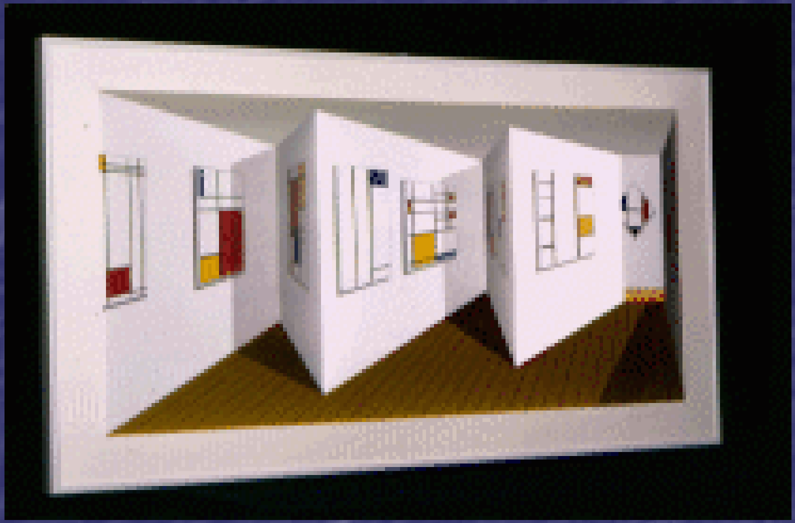
Whiteness from 3D structure



Zone B (shadowed by the green cylinder) seems whiter than zone A (unshadowed). However, both zones have the same objective luminous intensity (see right panel).

Adelson & Pentland (1996) The perception of shading and reflectance. In: Perception as Bayesian Inference (Knill & Richards, eds.) Cambridge University Press.

3D shape perception: the role of priors for regularity (perspective), rigidity (optic flow) and stationarity (self-motion)



Patrick Hughes « Reverspective »
http://www.patrickhughes.co.uk/

(the mental power test)

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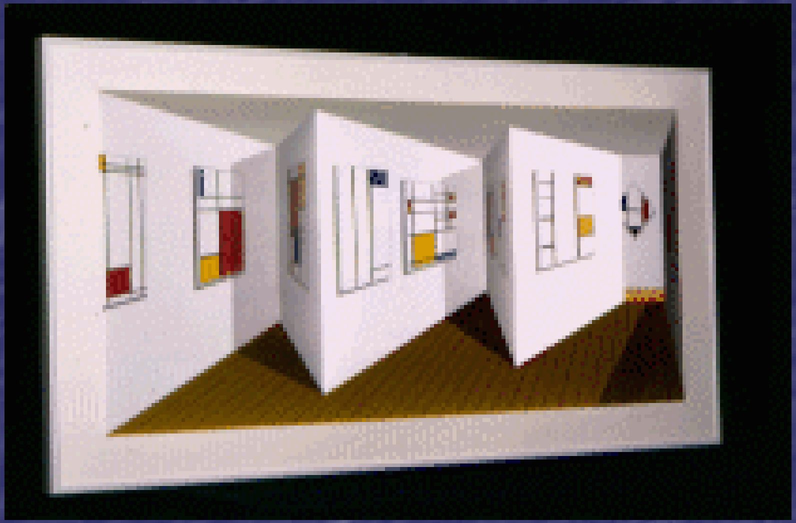

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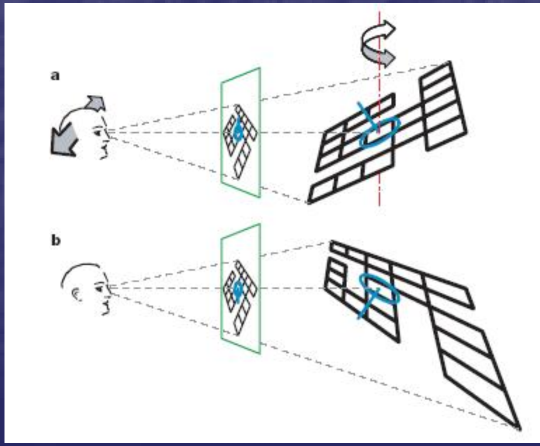
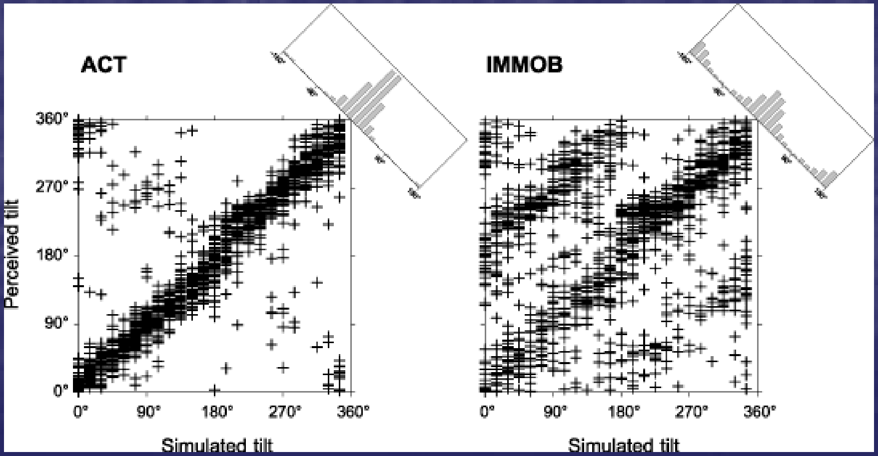
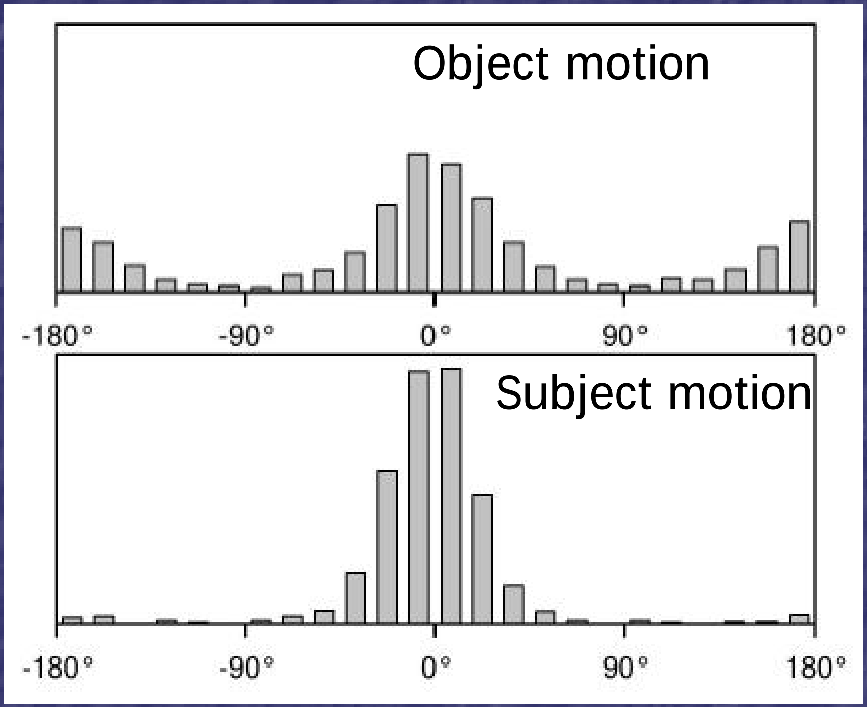




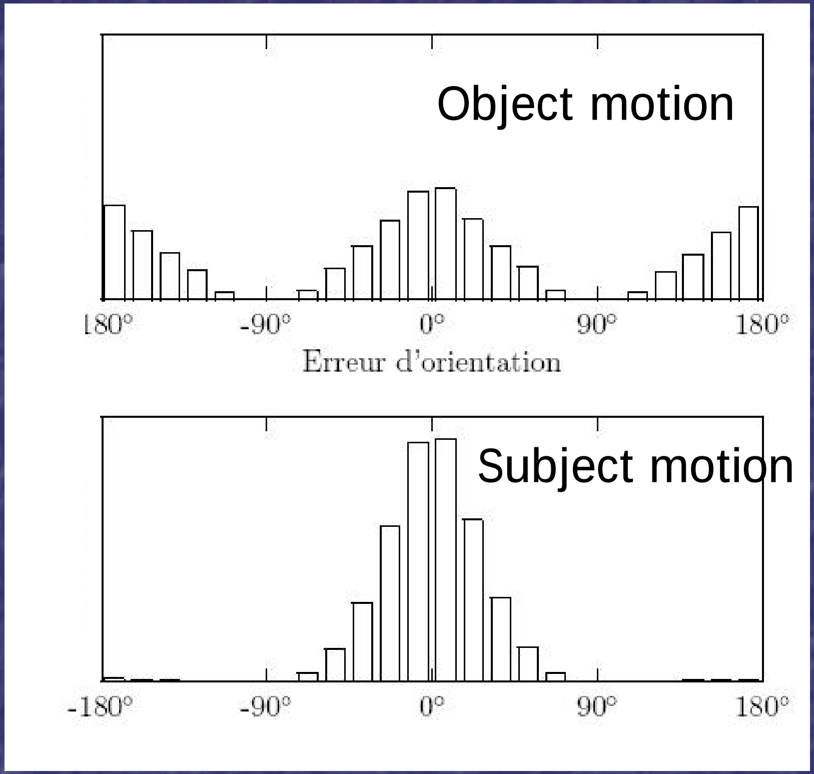
Wexler, Panerai, Lamouret & Droulez, *Nature* (2001)

Van Boxtel, Wexler & Droulez, *Journal of Vision* (2003)

Experiment



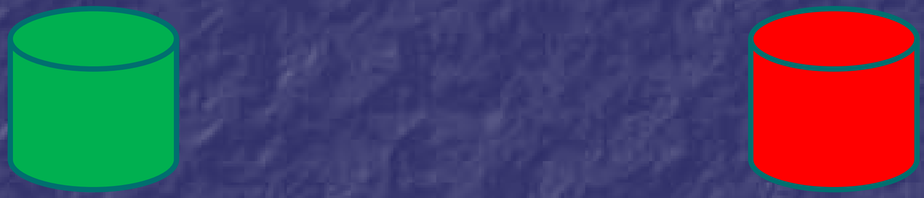
Model



Colas, Droulez, Wexler & Bessière (2007) *Biological Cybernetics*, 97:461-477

Probability Matching

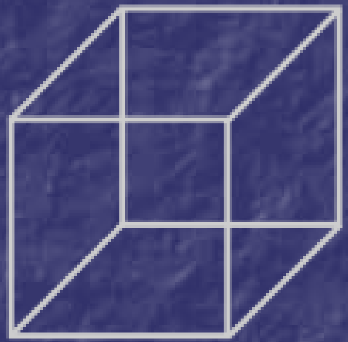
75 % 25 %

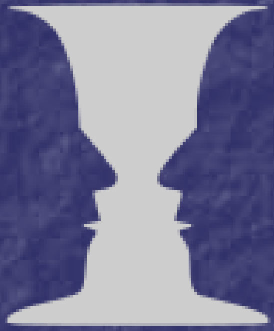


Koehler & James (2009) Probability matching in choice under uncertainty: Intuition versus deliberation. Cognition 113: 123

Variability in perception

- The problem in perception (e.g. 3D perception) is NOT to get rid of sensory noise, but to solve ambiguities and indeterminacies.





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- Question: why perceptive or motor responses exhibit a large variability from trial to trial, or from time to time ?

- Could individual subject responses be "samples" drawn from an internally estimated probability distribution ?

The Bayesian Brain

- How probability distributions are represented in the brain ?
- How Bayesian inferences are performed by neurons ?

A variety of theoretical propositions

Explicit

- Direct code : single neurone activity ↔ one probability value

$r \approx P(S = s)$ …. $r \approx \mathrm{Log}(P(S = s))$ … $r \approx \mathrm{Log}(P(S = 1) / P(S = 0))$

Anastasio et al (2000); Gold & Shadlen (2001); Rao (2004); Yang & Shadlen (2007); …

- Population code : ensemble of neurones ↔ linear combination of a set of basis functions

$P(S = s) \approx \Sigma_i r_i.h_i(s)$ or $\mathrm{Log}(P(S = s)) \approx \Sigma_i r_i.h_i(s)$

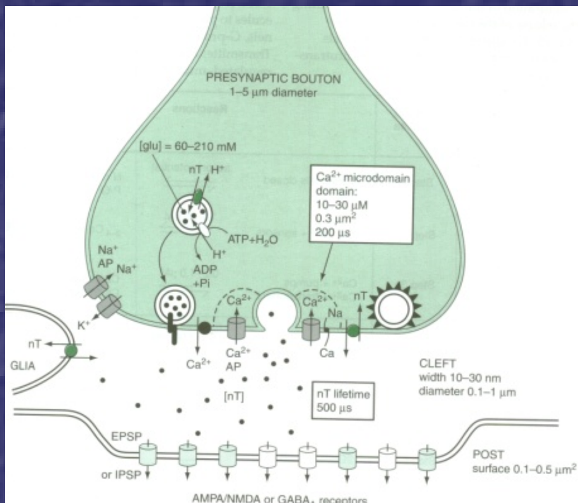
Zemel, Dayan & Pouget (1998); Ma, Beck, Latham & Pouget (2006); …

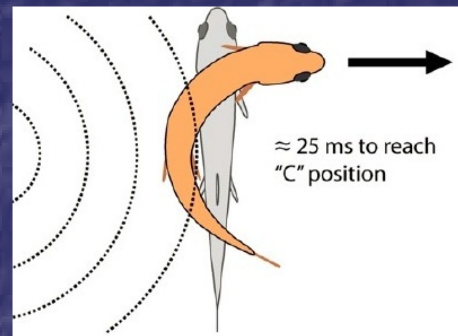
Implicit

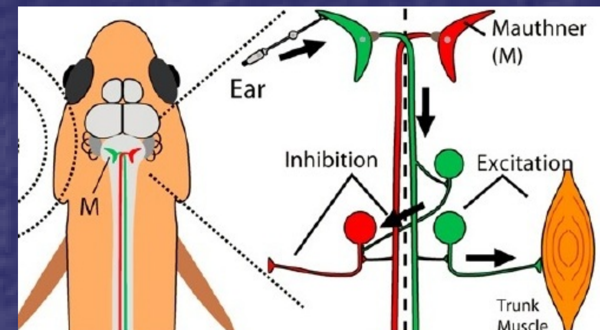
- Sampling code: instantaneous population activity ↔ random draw from a probability distribution

Lee & Mumford (2003); Fiser et al (2010); Maass (2014); …

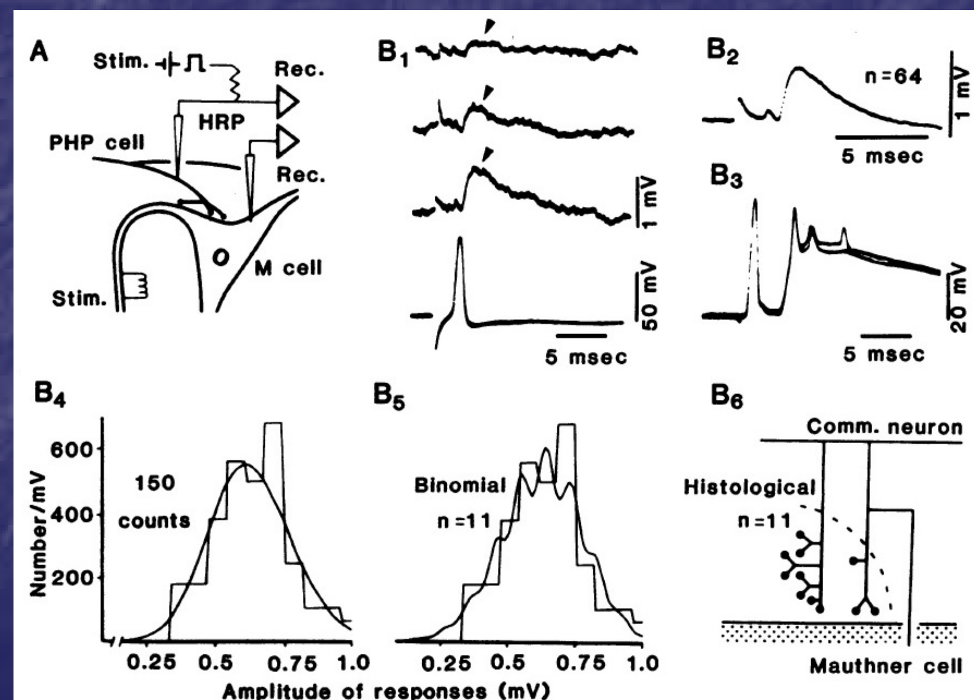
And a variety of sources of stochasticity in neural activity





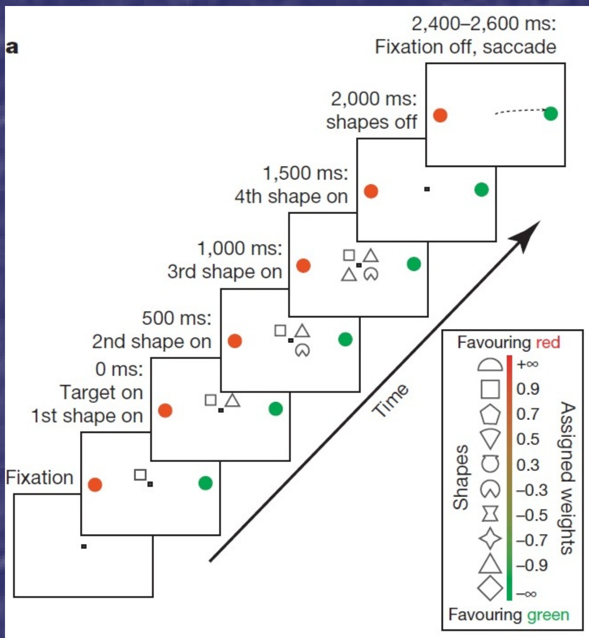


One of the main source:
the probabilistic release of
neurotransmitter



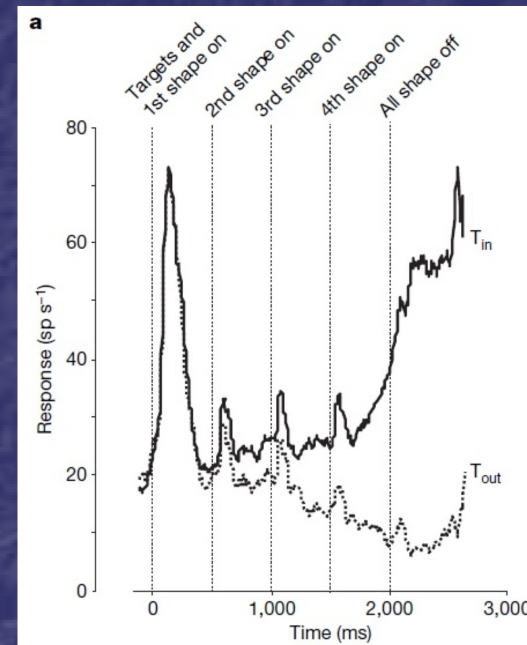
Data and model from Korn et al, Science 213 (1981)

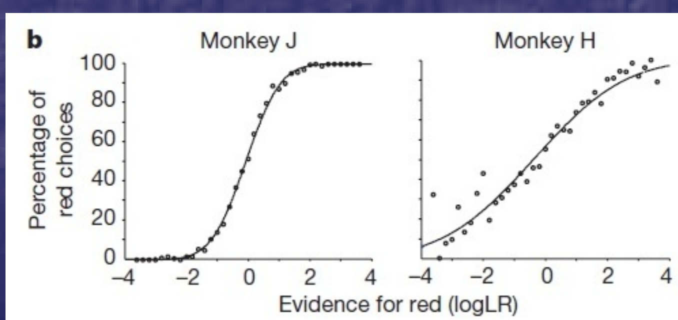
Evidence for a direct code (Log Likehood Ratio)

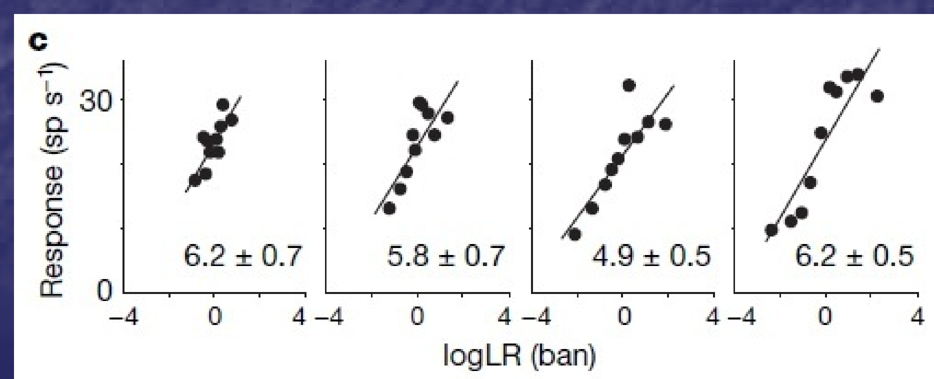


Accumulation of evidence (in LLR)

Activity in LIP (overtrained monkeys)



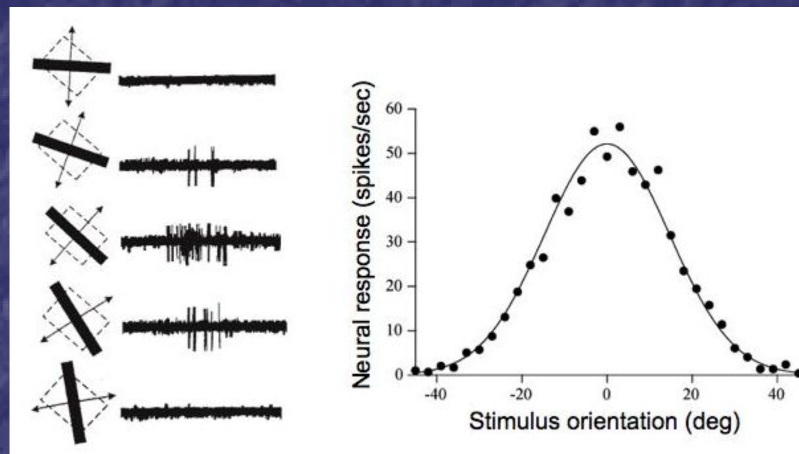




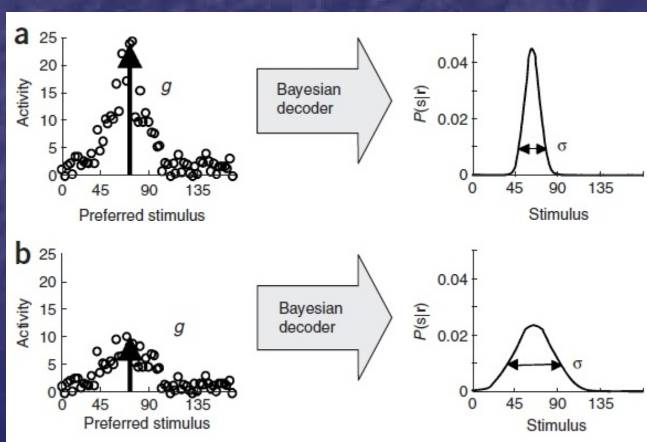
But LLR and P(Choice) are highly correlated !

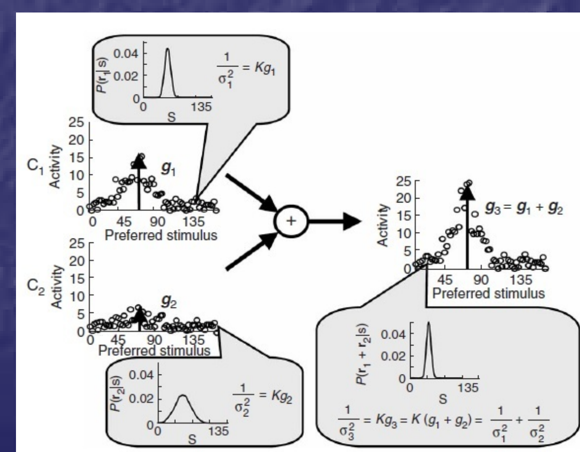
Yang & Shadlen, *Nature* 447 (2007)

Evidence for a population code (Tuning curves)



In cats: Hubel & Wiesel, J. Phys. (1959). In monkeys: Hubel & Wiesel, J. Phys. (1968)

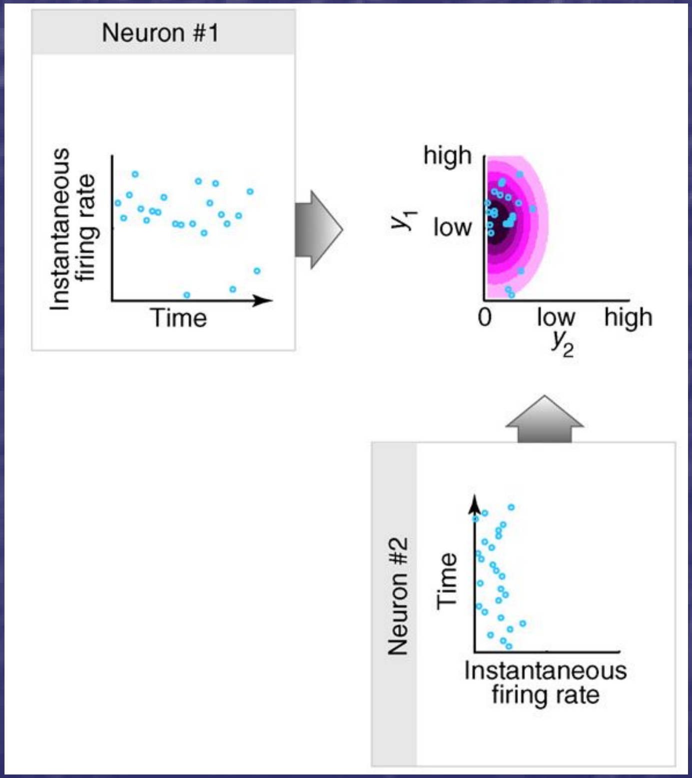




Ma, Beck, Latham & Pouget, *Nature Neurosc.* 9:1432 (2006)

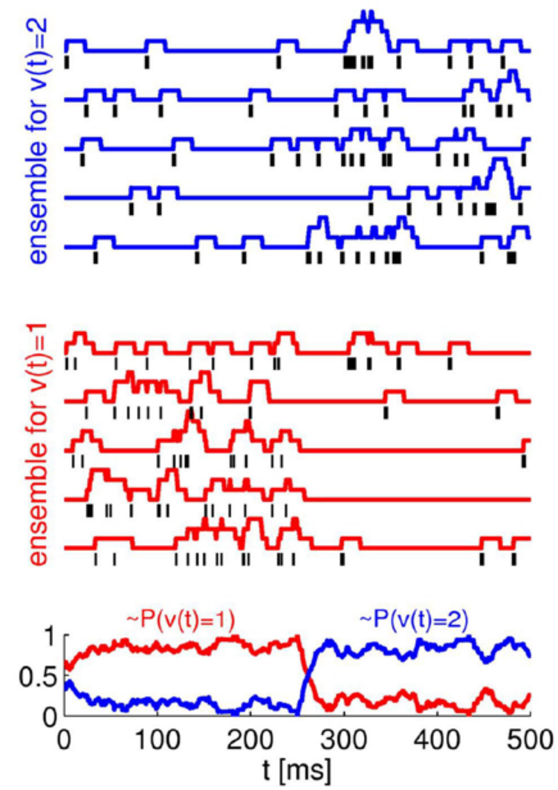
Neural noise: an essential ingredient for probabilistic inference ?

One neuron per (discrete) variable



Fiser et al, Trends in Cognitive Sc. 14 (2010)

One population per (binary) variable



Legenstein & Maass, PLoS CB (2014)

● Direct codes and population codes aim at representing explicitly the probability distributions. Computation is based on exact inference (or close to exact inference). Neural “noise” is conceived as a nuisance. Might be not suited for solving problems in high dimension spaces.

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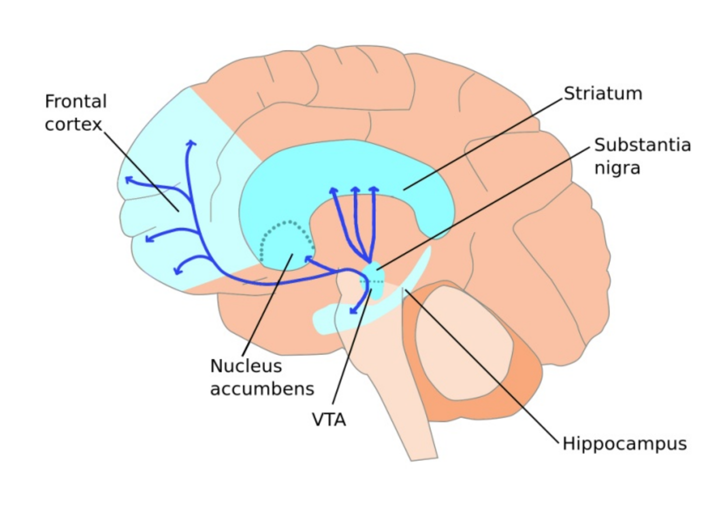
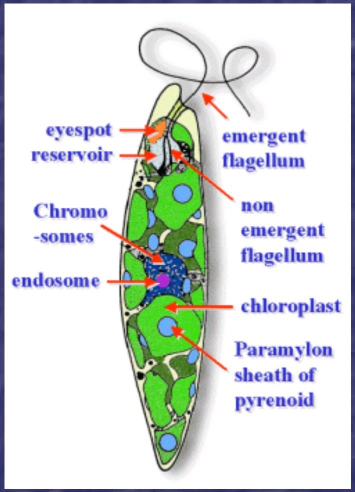
- Sampling code: accounts for biological stochasticity, well suited for hard inference problems. But the relevance of known sampling approach (e.g. MCMC) in neurobiology has yet to be demonstrated.

The Bayesian Cell

Neuronal activity is also controlled by complex biochemical networks

Unicellular organisms have also developed well adapted behaviors in spite of uncertain environment



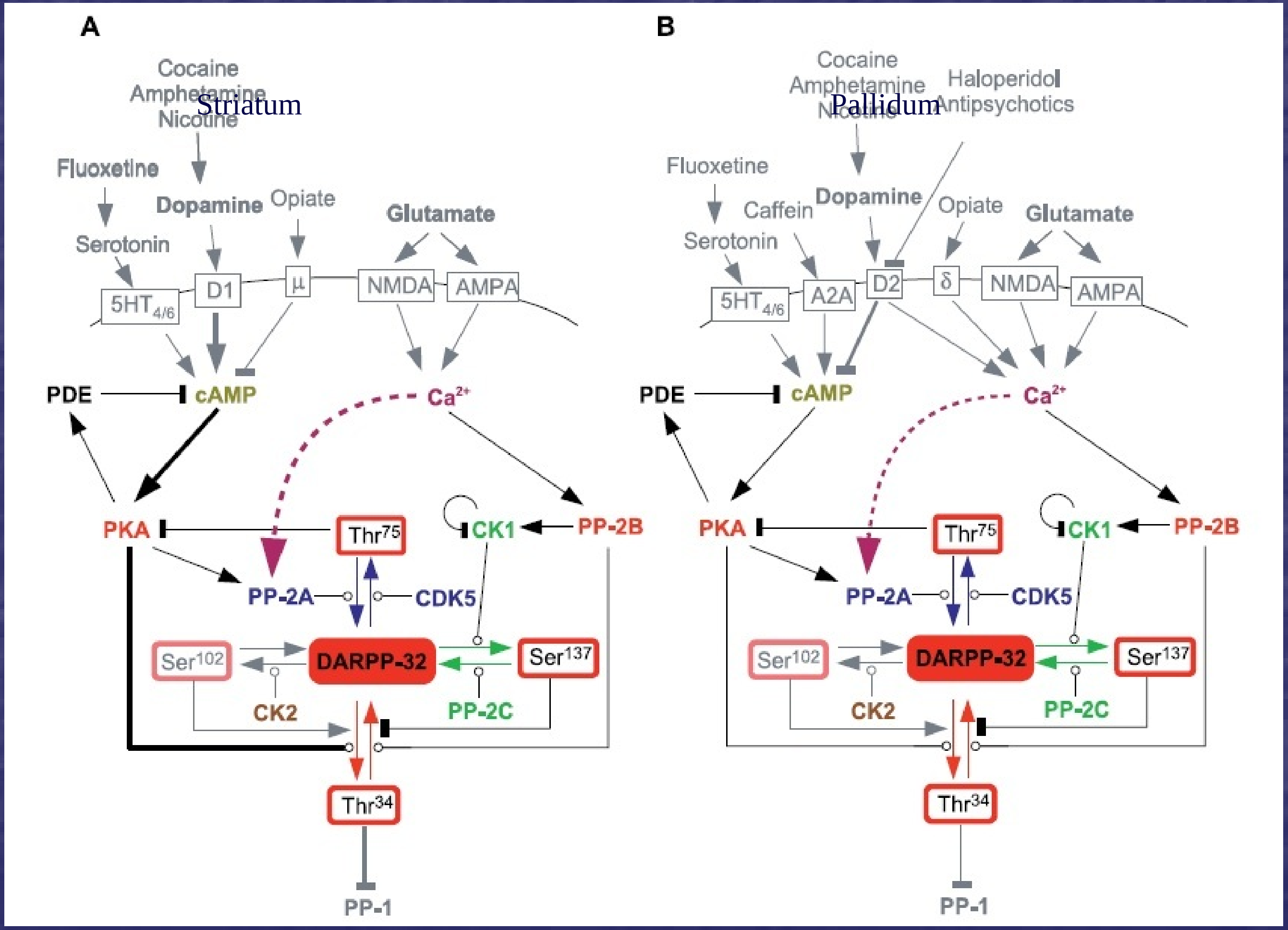


Euglena

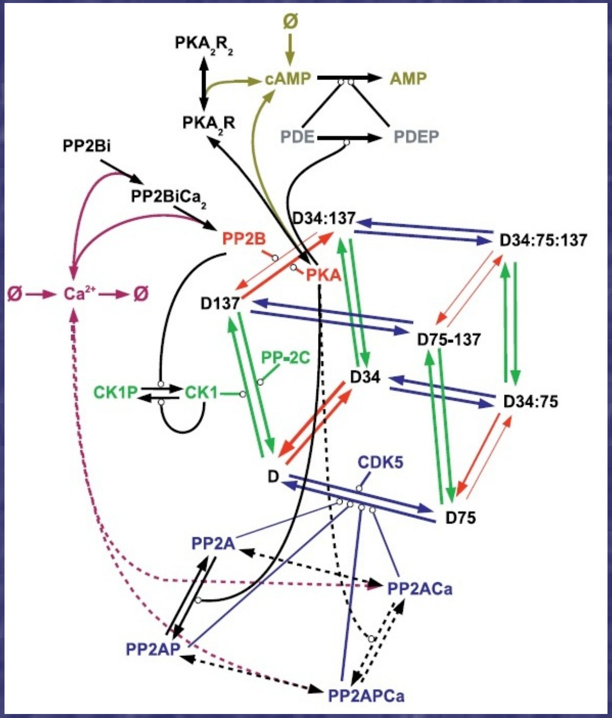
Chlamydomonas

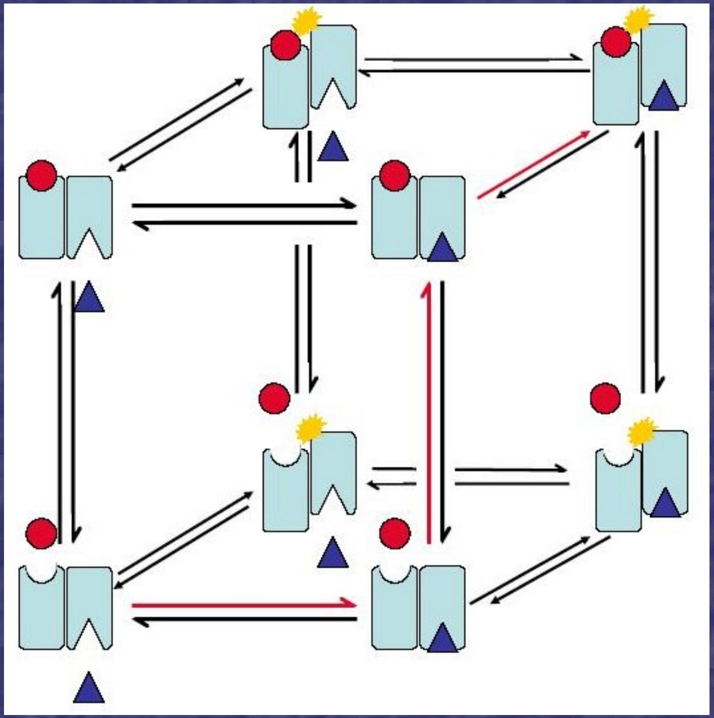
Integration of dopamine and glutamate signals in neurons of the basal ganglia (striatum and pallidum), role in reinforcement learning. Frank et al, Nature Neurosc. (2009)

Perkins & Swain, Strategies for cellular decision-making, Mol. Syst. Biol, (2009)



Fernandez et al, DARPP32 is a robust integrator of Dopamine and Glutamate Signals. PLoS Comp. Biol. (2006)

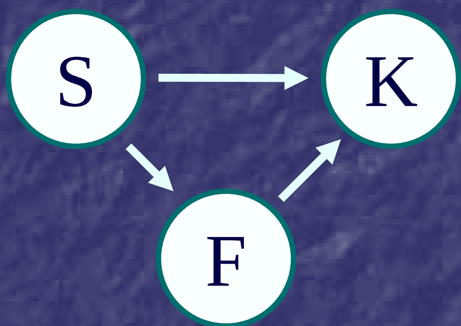




DARPP32:
3 sites of phosphorylation → 8 states
Fernandez et al (2006)

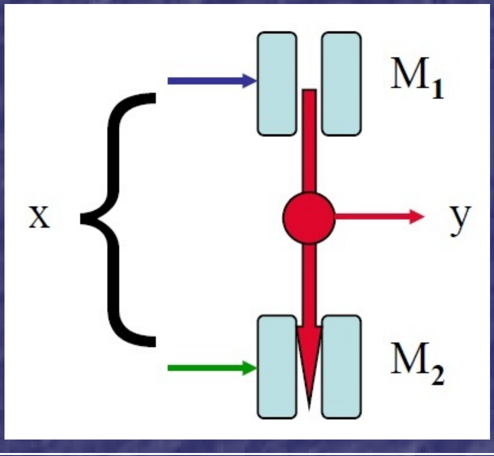
A Markov model of allosteric transitions
Droulez et al (2015)

Equivalence between Bayesian inference and cascades of biochemical systems



$$\frac{P([S=s]\,|\,k)}{P([S=0]\,|\,k)} = \frac{\sum_F P([S=s],F) \times P(k\,|\,[S=s],F)}{\sum_F P([S=0],F) \times P(k\,|\,[S=0],F)}$$

The output probability quotient is a rational function (with non negative coefficients) of likelihood quotients.

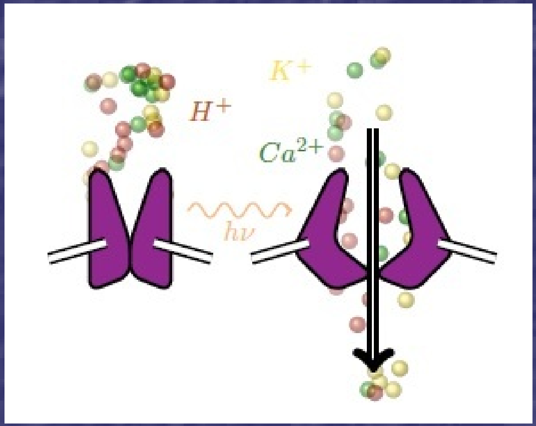


Markov model of an biochemical module:
N_Y = number of second messengers
$\Phi_1(x)$ = rate of release (by M_1) : a RFNC of x
$\varphi_2(x)$ = rate of removal per messenger (by M_2)
$\Rightarrow$ At equilibrium $P(N_Y)$ is a Poisson distribution of parameter $\lambda(x) = \Phi_1(x) / \varphi_2(x)$

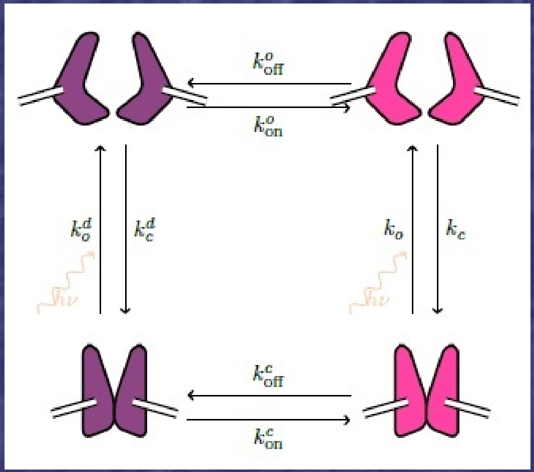
The output concentration y is a RFNC of x.

Towards a Bayesian model of sensory-motor behavior in unicellular organisms

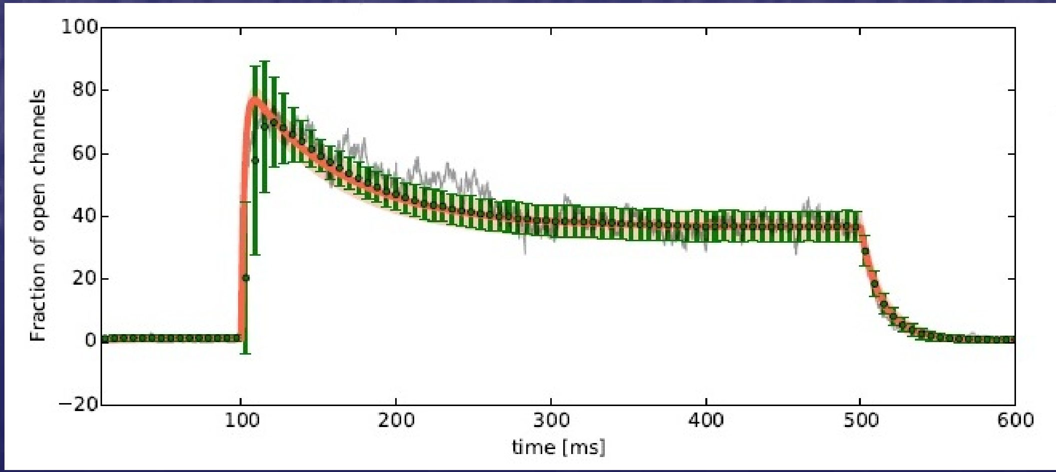
Channelrhodopsin: the molecular light sensor in the eyespot



Markov model of Channelrhodopsin (4 states)

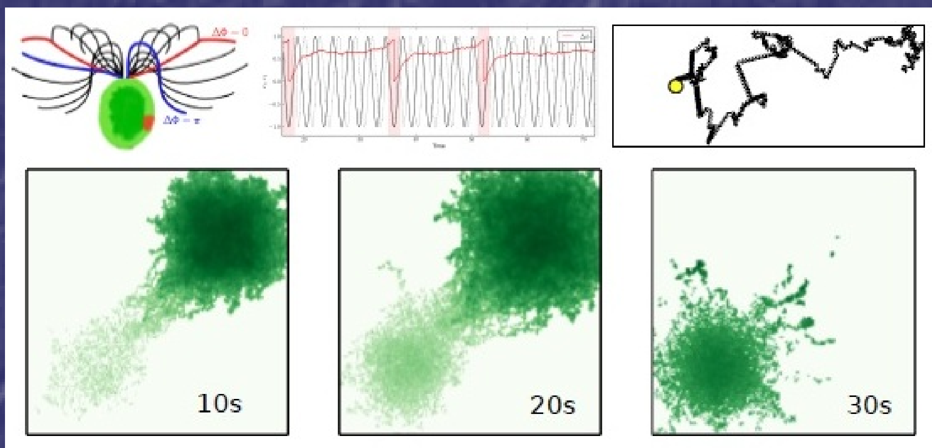


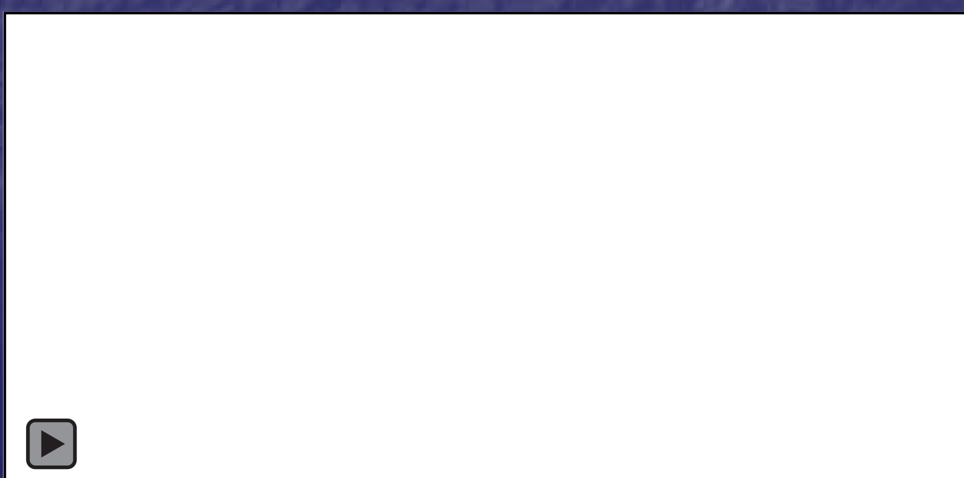
Example of simulation (Colliaux, Bessière & Droulez, 2014)



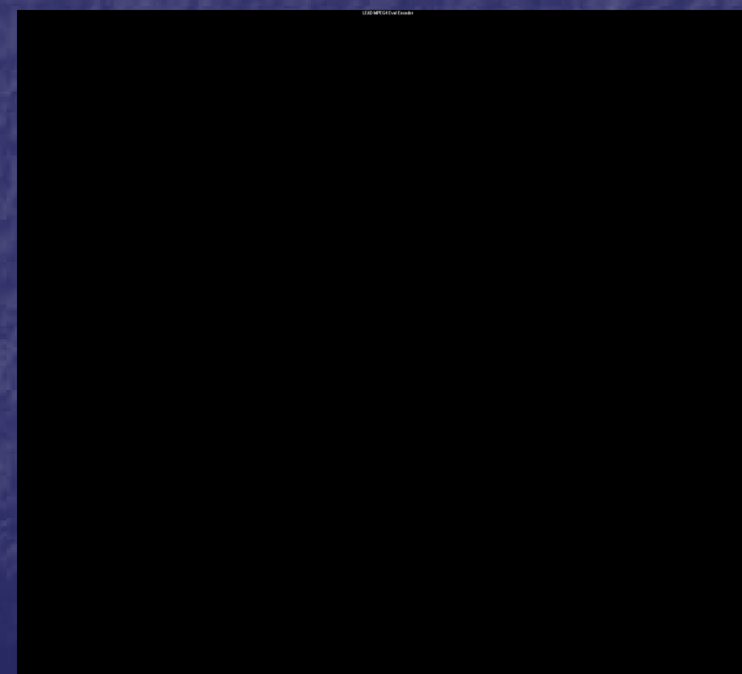
Towards a Bayesian model of sensory-motor behavior in unicellular organisms

Simulation of phototaxis behavior (Colliaux et al, ECAL 2015)





Experimental results



The Bayesian cell hypothesis

- In complement to the usual neurocomputational approach (e.g. integrate-and- fire neurons), models of the underlying biochemical signaling networks are required to understand how the brain could perform Bayesian computing.

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- The equivalence between Bayesian inferences and the behavior of large populations of macromolecules involved in cell signaling opens new perspectives to understand how single cells and unicellular organisms could process uncertain information.

CONCLUSION

1. Bayesian theory of perception and behavior : a success story.

2. Variability in behavior and variability in the way brain and cell process information.

3. Is variability a “noise” due to non reliable functioning of biological systems ?

4. Or, is variability a useful “ingredient” of Bayesian computing (for biological systems, but also for future artificial systems) ?

Thank you for your attention !