Advanced Neuroscience
Computational Track

NeuroTech track
Master in Bio Medical Engeneering - Paris Cité

9/09/2025 Dr. Quaresima Alessio

The ANC course

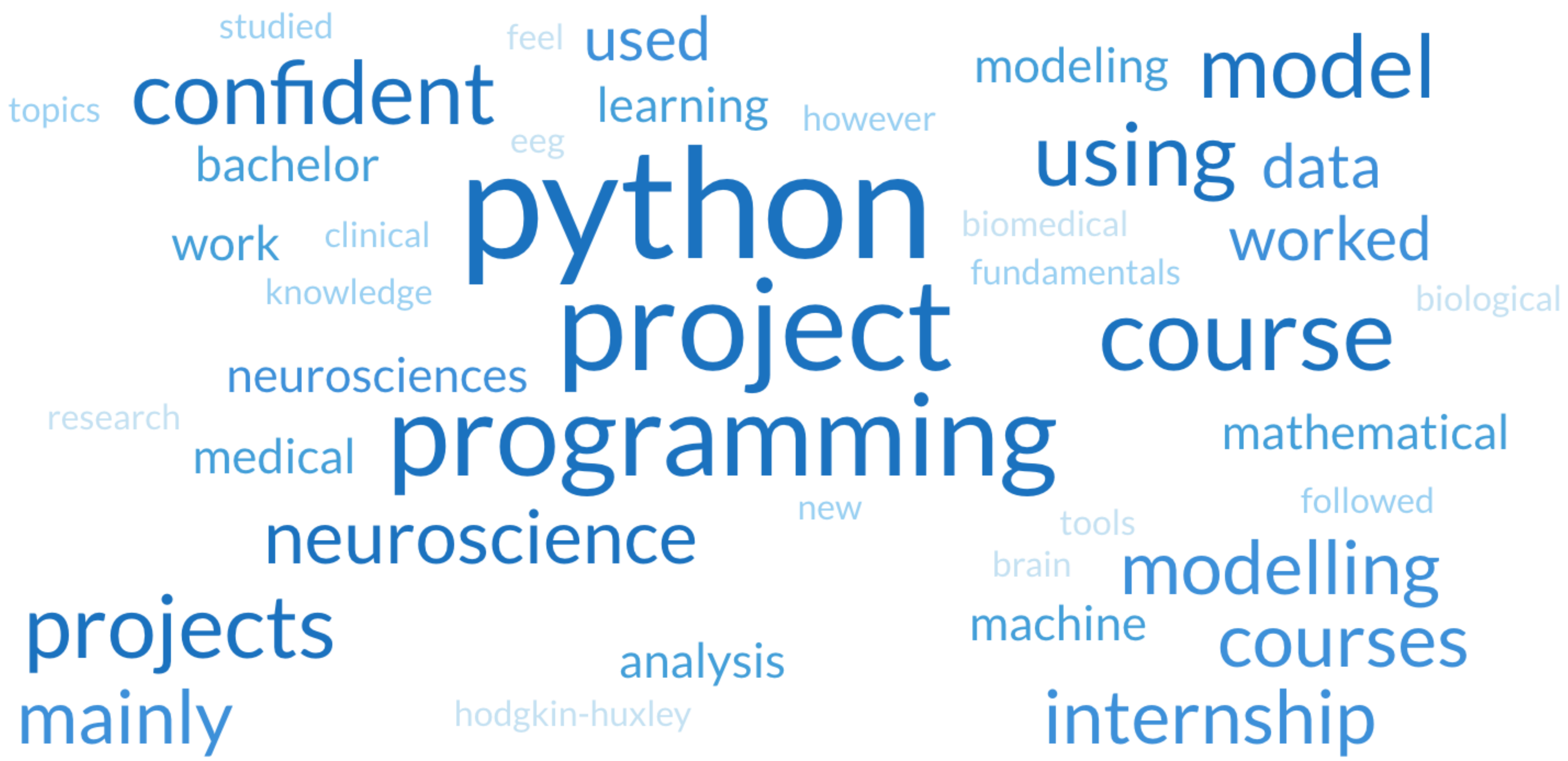
Structure and Organization
Students will engage in tutored group projects focusing on computational neuroscience fundamentals.

- tutored group projects that explore the fundamentals of computational neuroscience, including modelling, simulation, and related methodologies.

- Foundational knowledge will be developed through guided readings and critical discussions of the extensive scientific literature and available resources

Assessment
- Final project presentation (50%)
- Understanding shown during discussions and active participation (30%).
- The quality of technical implementation and coding (20%).

Students background and expectations



Calendar:

Week 1: Models in Comp Neuro
Mardi 09/09/2025 14-16
Jeudi 11/09/2025 14-16

Week 2: Simulations
Mardi 16/09/2025 14-16
Jeudi 18/09/2025 14-16

Week 3: Project tutoring I
Jeudi 25/09/2025 14-16

Week 4: Project tutoring II
Lundi 06/10/2025 14-16
Jeudi 09/10/2025 14-16

Lecture 1:

Computational neuroscience and modeling

Computational neuroscience is a subfield of neuroscience which utilizes *theoretical analysis, mathematical models and abstractions* of the brain to perceive the principles that control development, structure, physiology, emotional and cognitive processes of the nervous system.

The goal of mathematical models in computational neuroscience is to capture the main properties of a biological system at multiple spatiotemporal scales, from *membrane potentials, neurotransmitter function and topographic architecture to a psychological faculty like behavior or learning.*

Models: what are they good for?

- Knowledge synthesis
- Identifying hidden assumptions, hypotheses, and unknowns
- Mechanistic insights
- Retrieving latent information
- Serving as a test bench for medical interventions
- Guiding the design of useful experiments (quantitative predictions)
- Inspiring new technologies and applications

Marr’s levels of analysis

At the most conceptual level, a computational understanding answers questions about

What problem does the system solve?

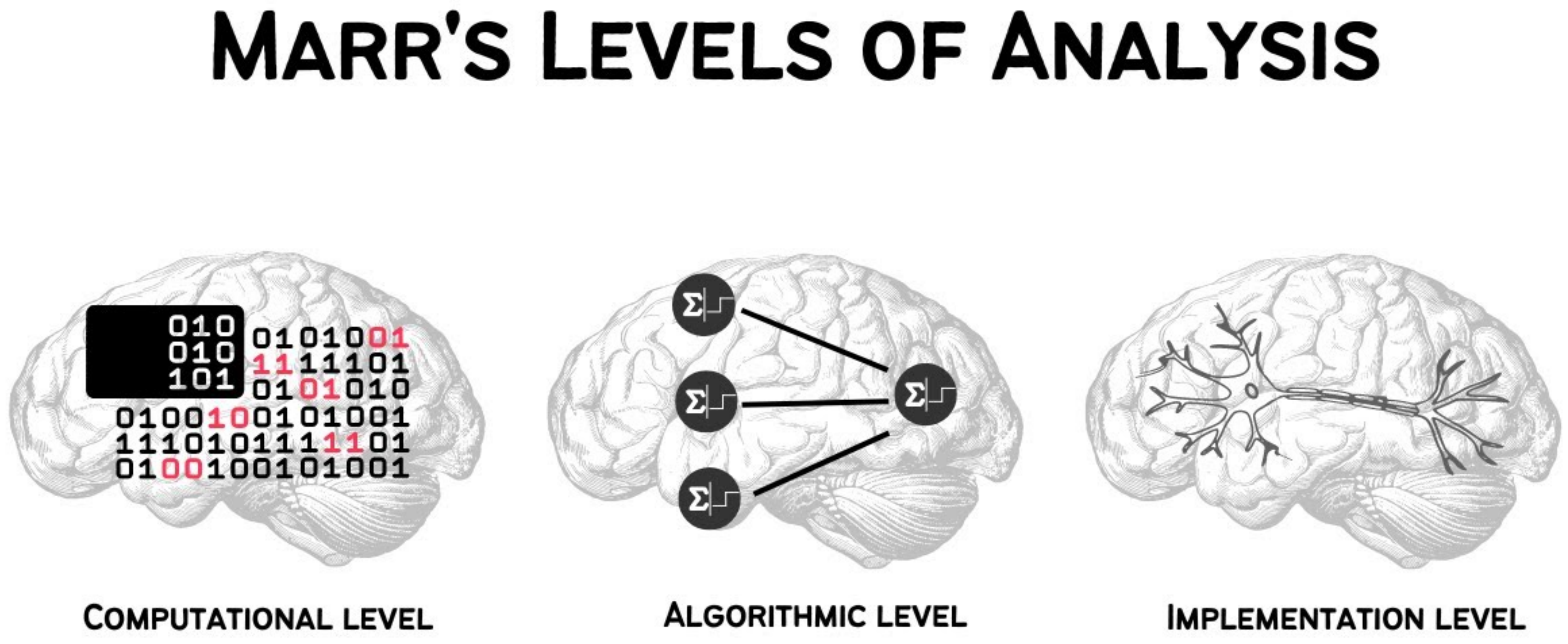
Why is the problem solved?

How does the system solve this problem?

Examples (not in order ;)
Which neural circuits in the primary visual cortex (V1) detect edges or orientation?

How does the visual system derive a stable, 3D representation of the world from 2D retinal images?

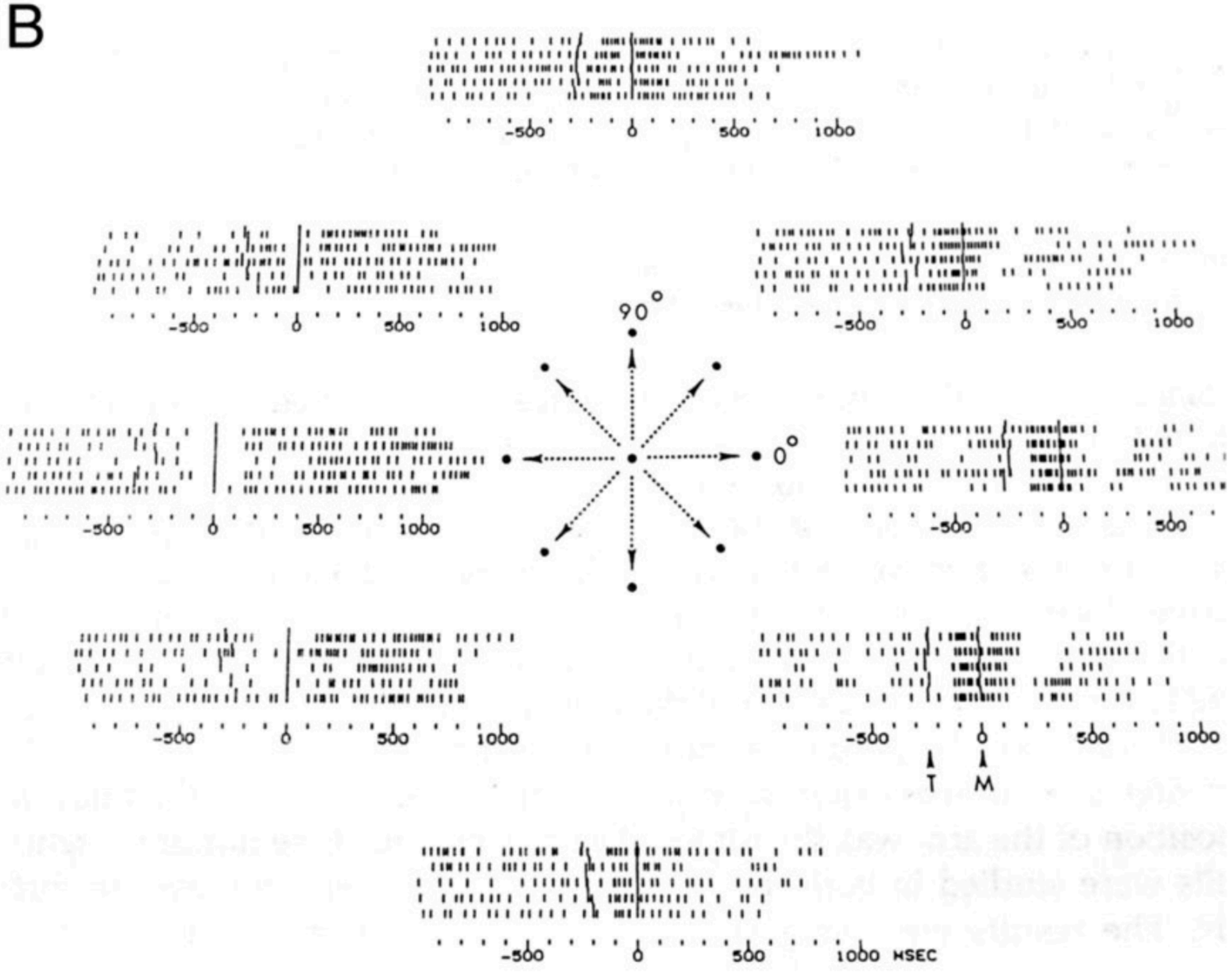
How does the visual system detect edges in an image?

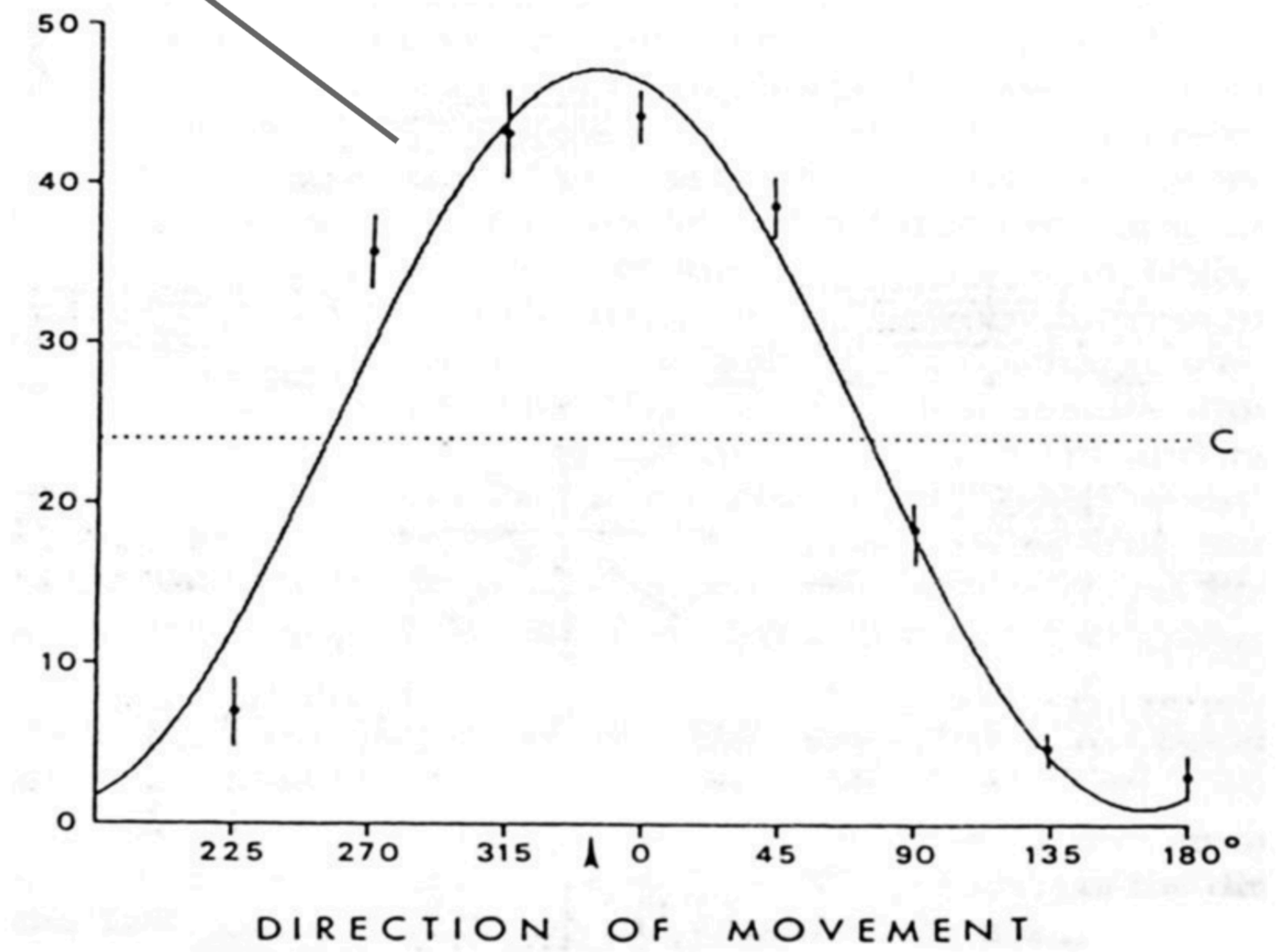


Computational level models

The cosine-tuning

$$\frac{f(s) - f_0}{f_{max}} = \cos(s - s_p)$$

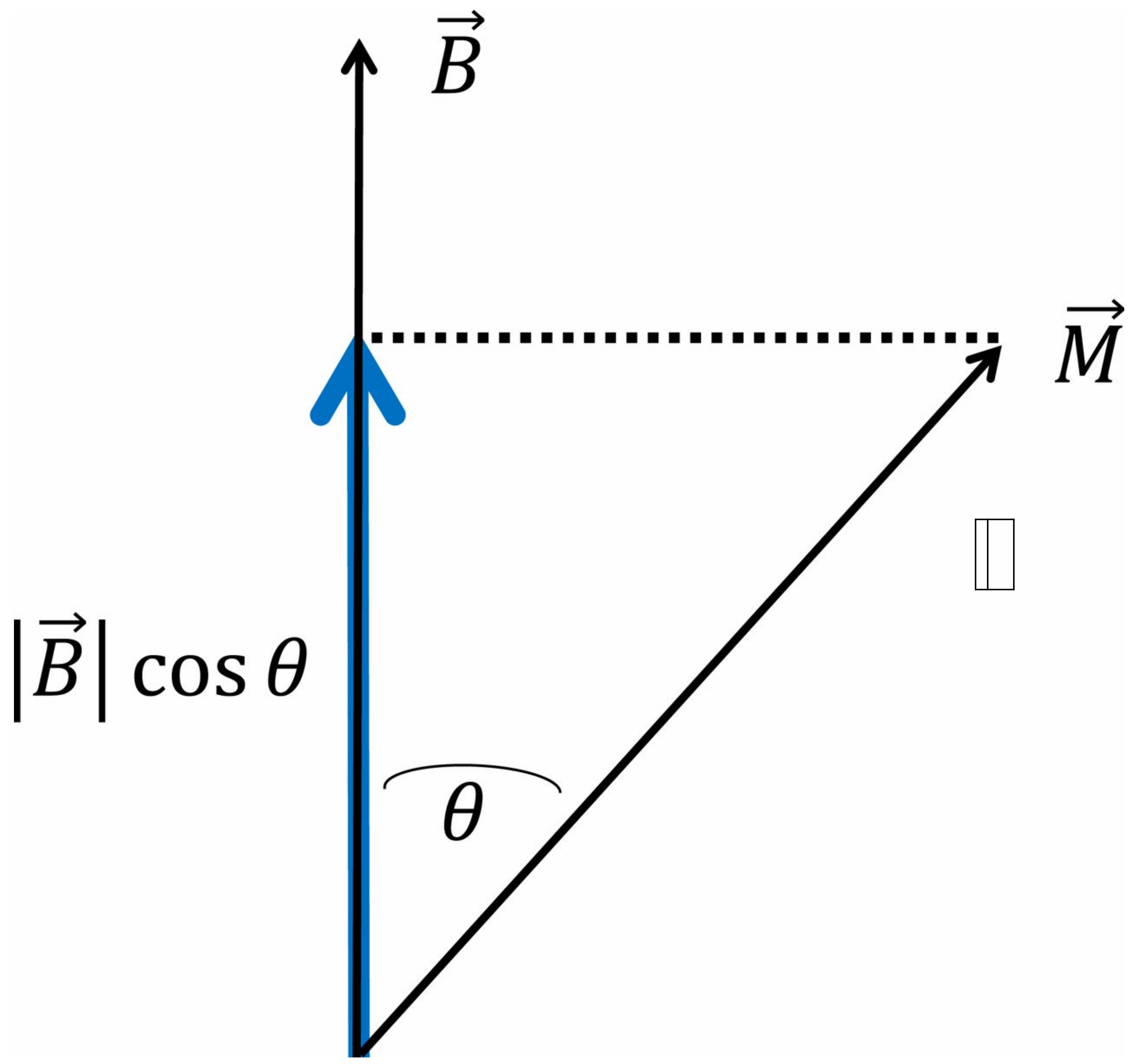




https://www.pnas.org/doi/10.1073/pnas.1902296116

Computational level models

The cosine-tuning -> scalar product tuning



$$FR = b_0 + b_x X + b_y Y,$$

The tuning principle can be visualized in terms of 2 vectors, **M** for movement direction and **B** that points in the preferred direction of a neuron. **M** is composed of *X* and *Y*, **B** has components *bx* and *by*. In a particular movement direction, the length **FR** will be proportional to the cosine of the angle between the neuron's preferred direction.

A conceptual advantage of the vector cartoon is that, although the dimensions of the 2 vectors will increase with the number of modeled variables, the equation itself always has the same form.

This feature has proven useful for extending the original 2-dimensional (2D) encoding models to 3 dimensions of arm movement, 3 dimensions of wrist movement, and 4 dimensions of hand shape. So that a total of 10 movement variables could be shown to be encoded in a single neuron's firing rate.

Computational level models

Advantages:

- Compact summary of data
- Generalizes across movements and sensory stimuli
- Applications in brain-machine interfaces (e.g., prosthetics)

Limitations:

- Purely descriptive
- No insight into how or why cosine tuning arises

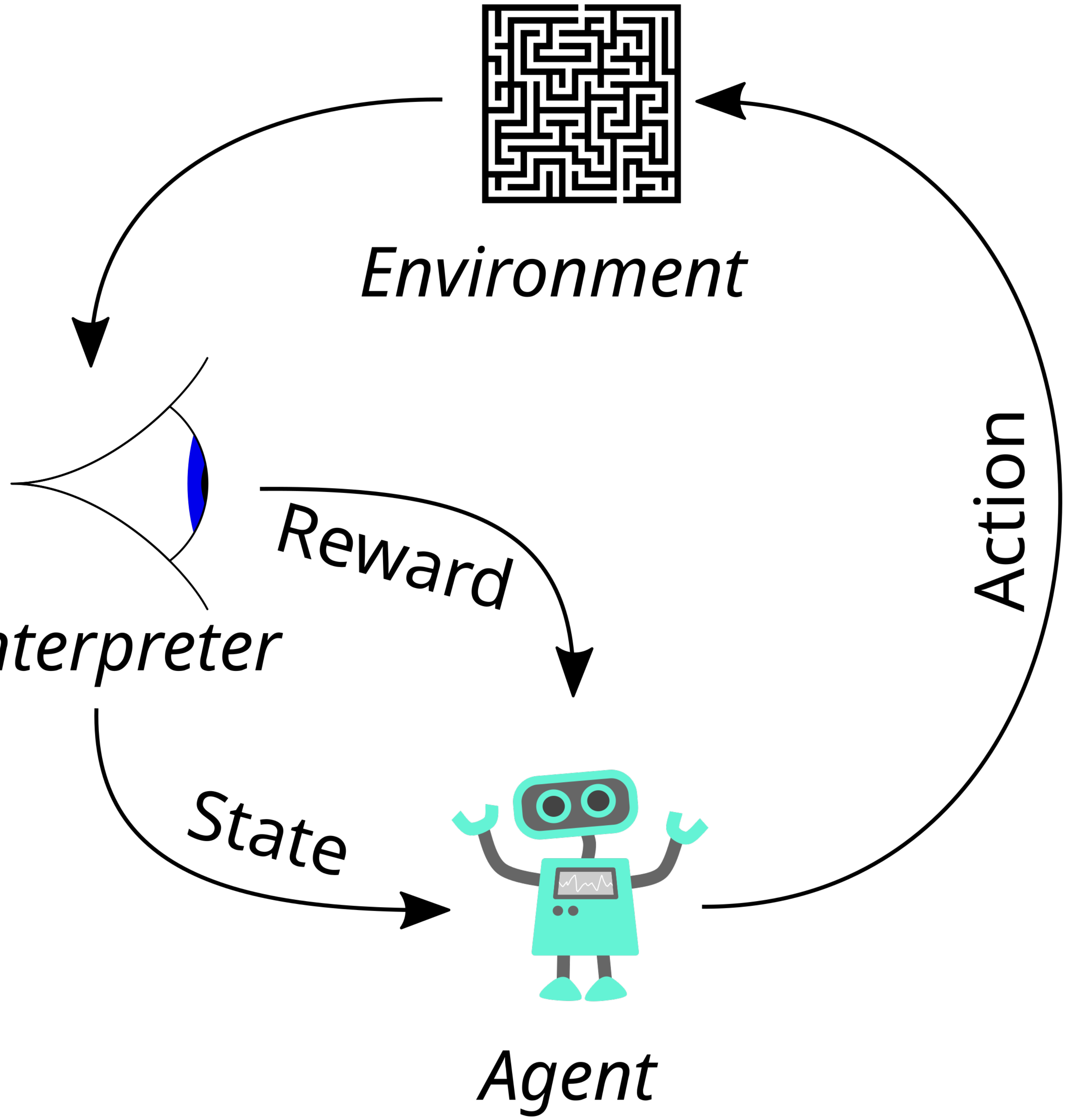
Algorithmic level models

Reinforcement Learning

- A set of environment and agent states (S);
- A set of actions of the agent (A);
- The transition probability (at time t) from state S to state S' under action A:

$$P_a(s,s') = \Pr(S_{t+1}{=}s' \mid S_t{=}s, A_t{=}a),$$

- The immediate reward after transition from S to S' under action A: $R_a(s,s')$



Algorithmic level models

Reinforcement Learning

- The agent can compute the value of a state:

$$v_\pi(s) = \mathbb{E}_\pi\left[R_{t+1} + \gamma R_{t+2} + \gamma^2 R_{t+3} + \dots \mid S_t = s\right]$$

Expected

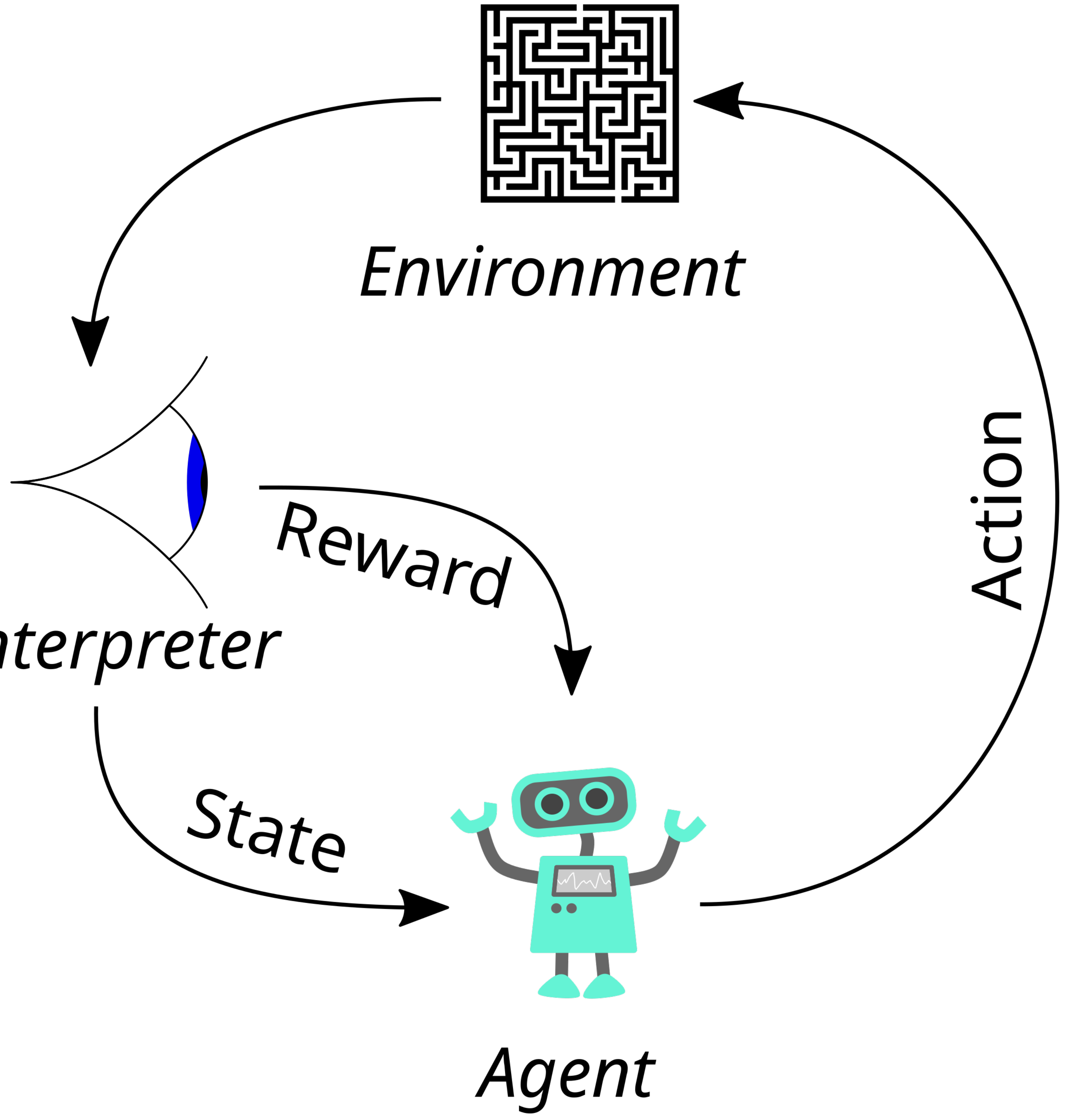
Reward
discounted

Given that state

- And take action based on a policy:

$$\pi : \mathcal{S} \times \mathcal{A} \to [0,1]$$
$$\pi(s,a) = \Pr(A_t{=}a \mid S_t{=}s)$$

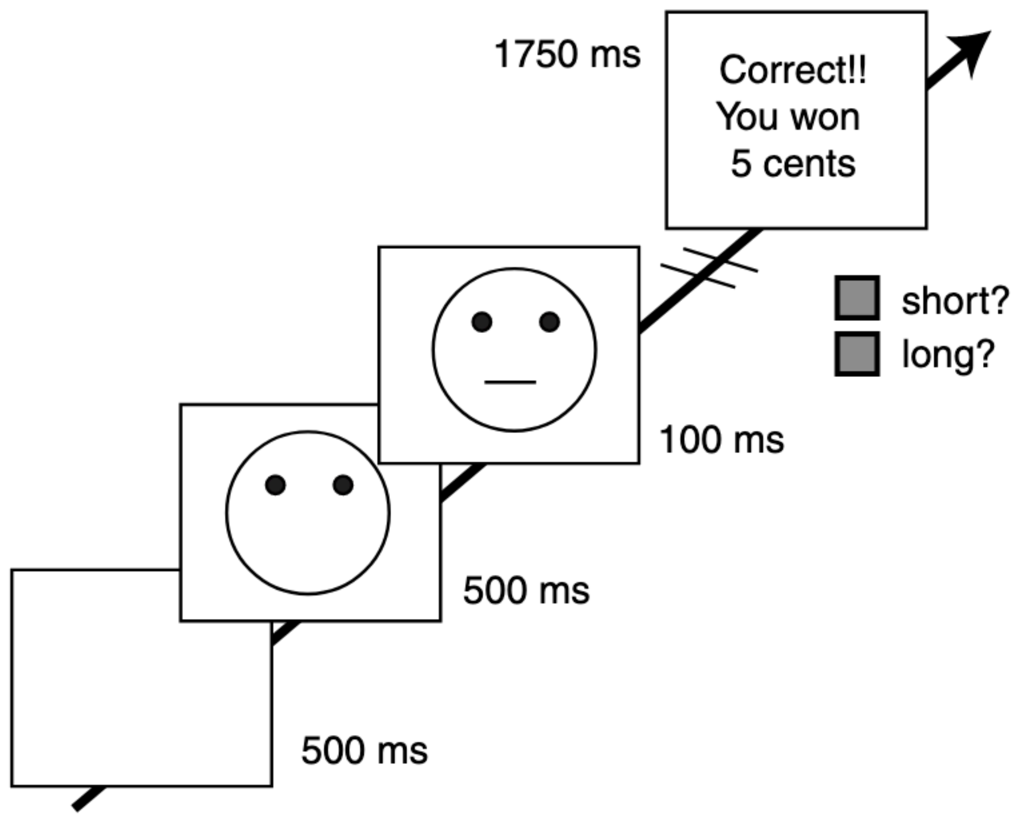
- The goal is to find the policy that maximizes the reward function *over time*



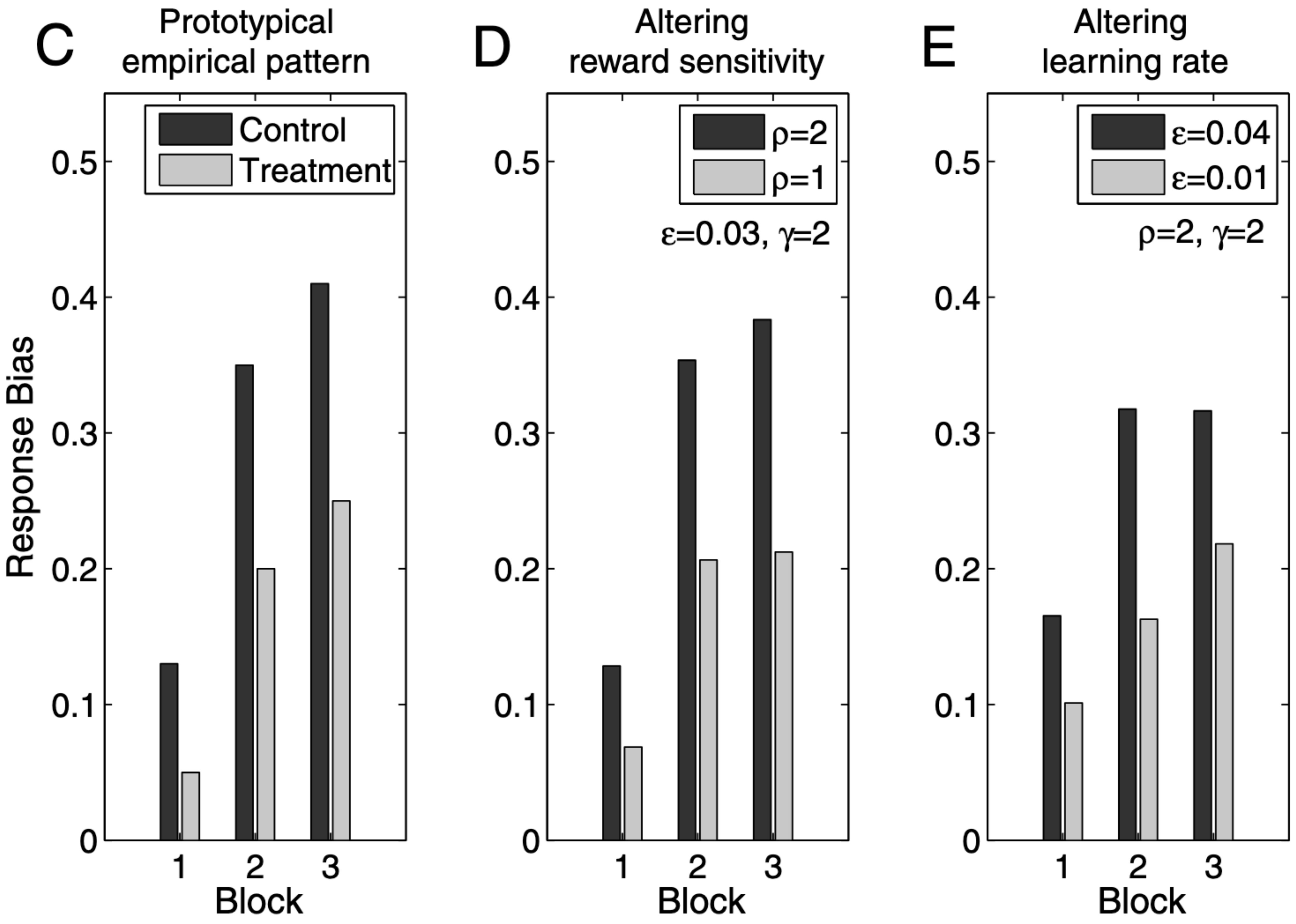
Algorithmic level models

Reinforcement Learning

Several studies have shown associations of anhedonia with reduced learning from rewarding outcomes



Long = rich:	Long correct:	75% rewarded
	Short correct:	30% rewarded
Short = rich:	Long correct:	30% rewarded
	Short correct:	75% rewarded

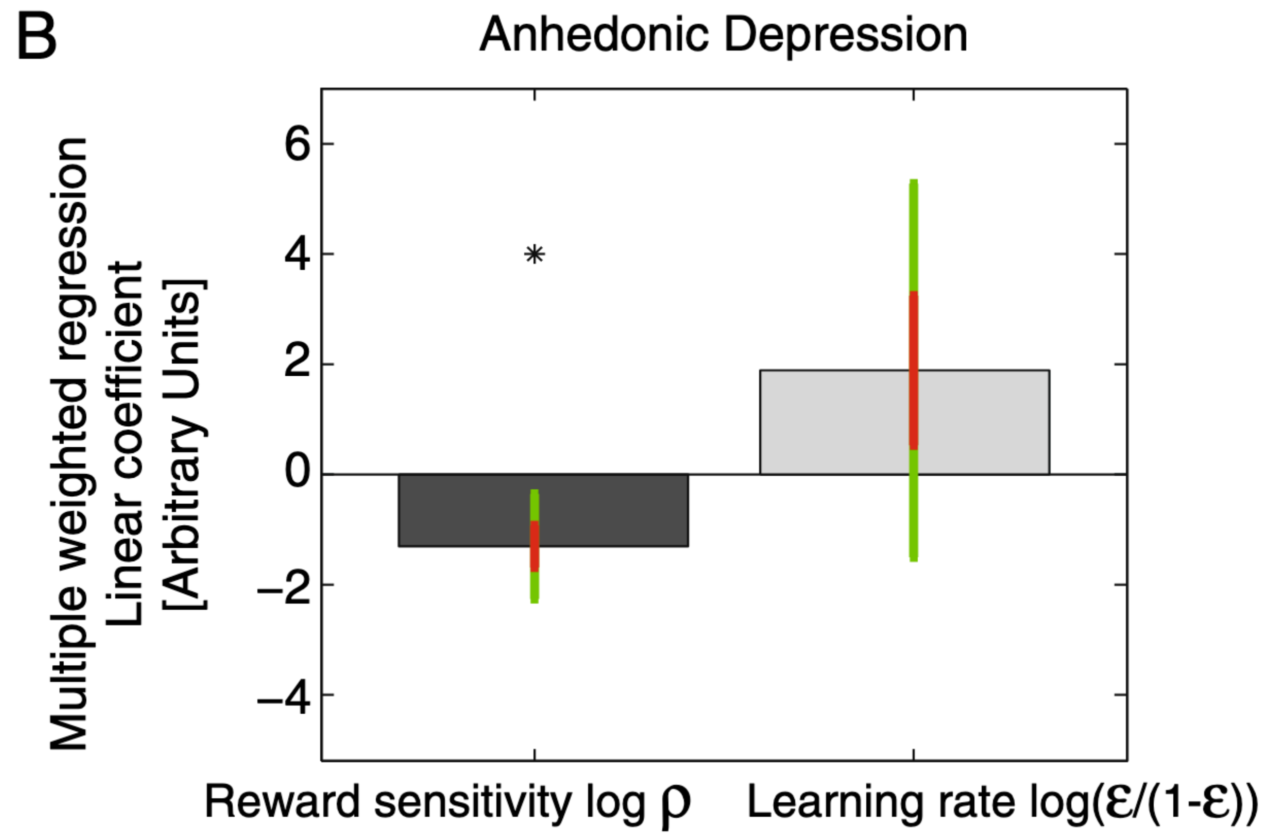


Prediction error

$$\delta_t = \rho r_t - \mathcal{Q}_t(a_t, s_t)$$

Values update

$$\mathcal{Q}_{t+1}(a_t, s_t) = \mathcal{Q}_t(a_t, s_t) + \epsilon \delta_t$$



https://biolmoodanxietydisord.biomedcentral.com/articles/10.1186/2045-5380-3-12

Computational level models

Description:

- Normative model for optimal behavior based on rewards and actions.

Advantages:

  - Provides a benchmark for optimal behavior
  - Synthesizes behavioral and neural data
  - Describes latent variables (e.g., reward prediction error)
  - Inspires modern AI technologies

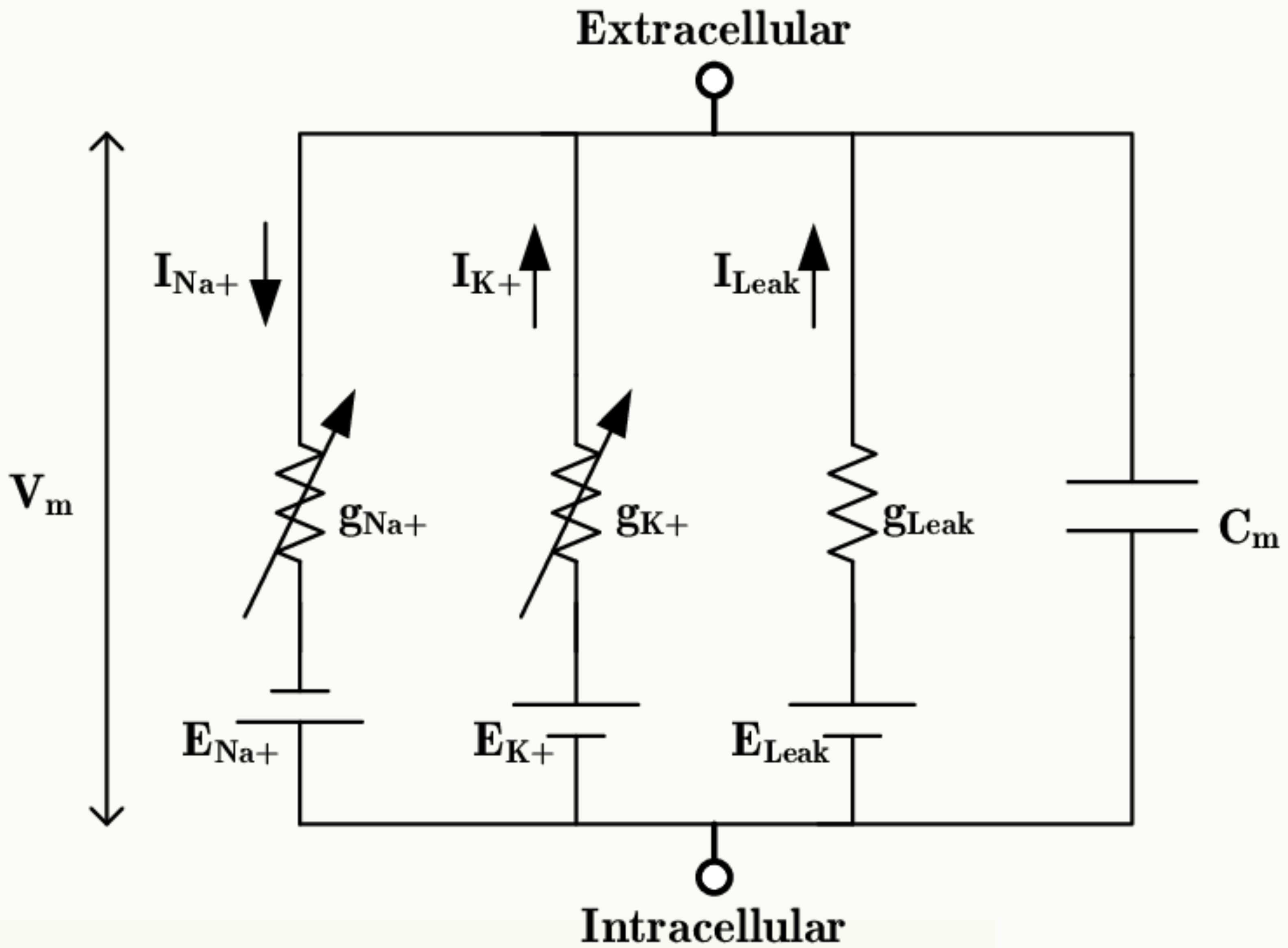
Limitations

  - Does not explain how the brain achieves reinforcement learning

Implementation level models

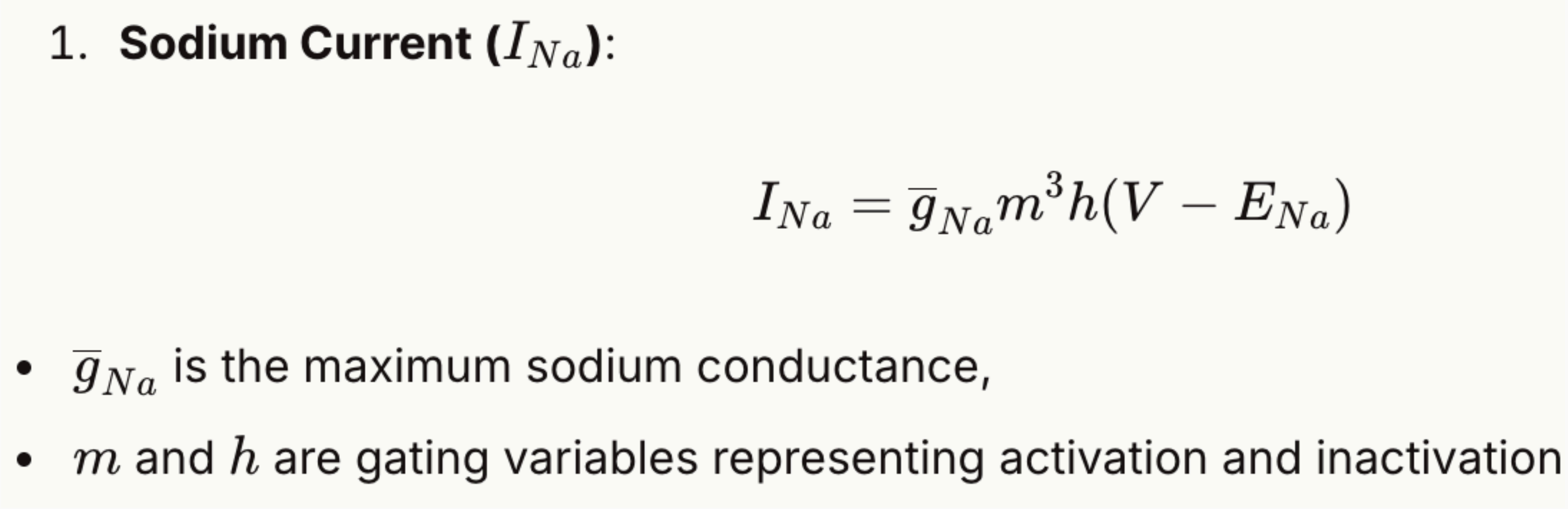
Hodgkin and Huxley

It describes the dynamics of the membrane potential:



$$C_m \frac{dV}{dt} = -I_{ion} + I_{ext}$$

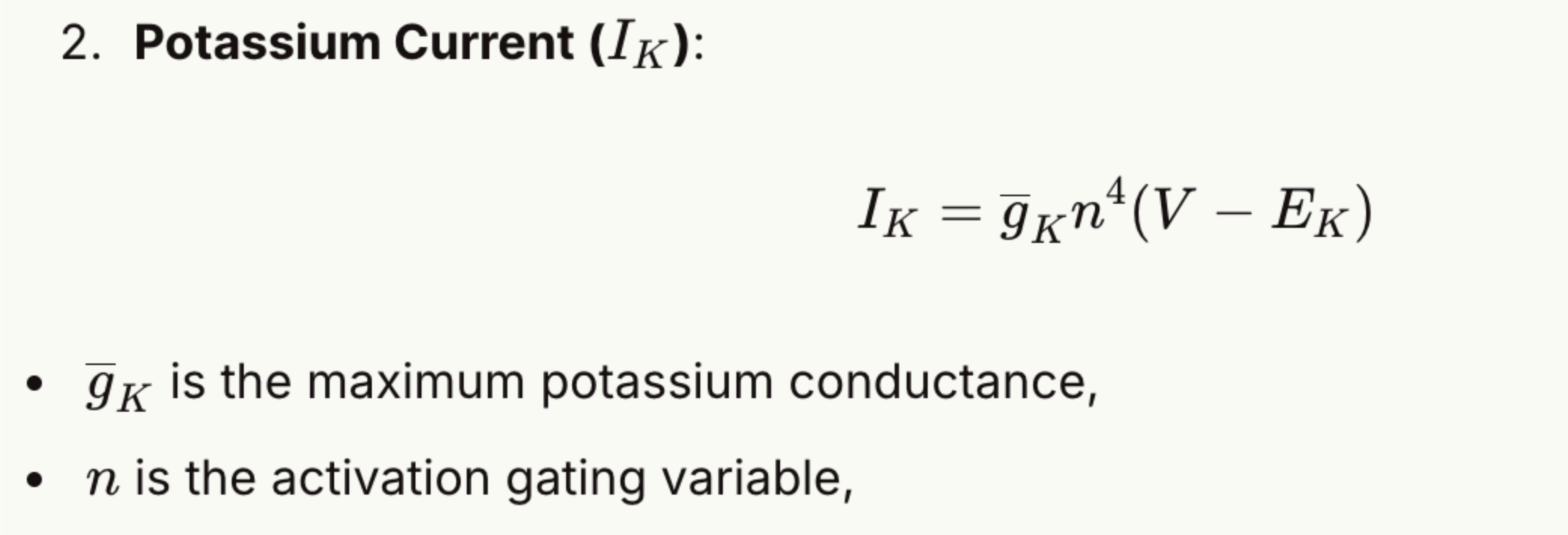
- C_m is the membrane capacitance,
- I_{ion} represents the total ionic current,
- I_{ext} is an externally applied current.



1. **Sodium Current (I_{Na}):**

$$I_{Na} = \overline{g}_{Na} m^3 h (V - E_{Na})$$

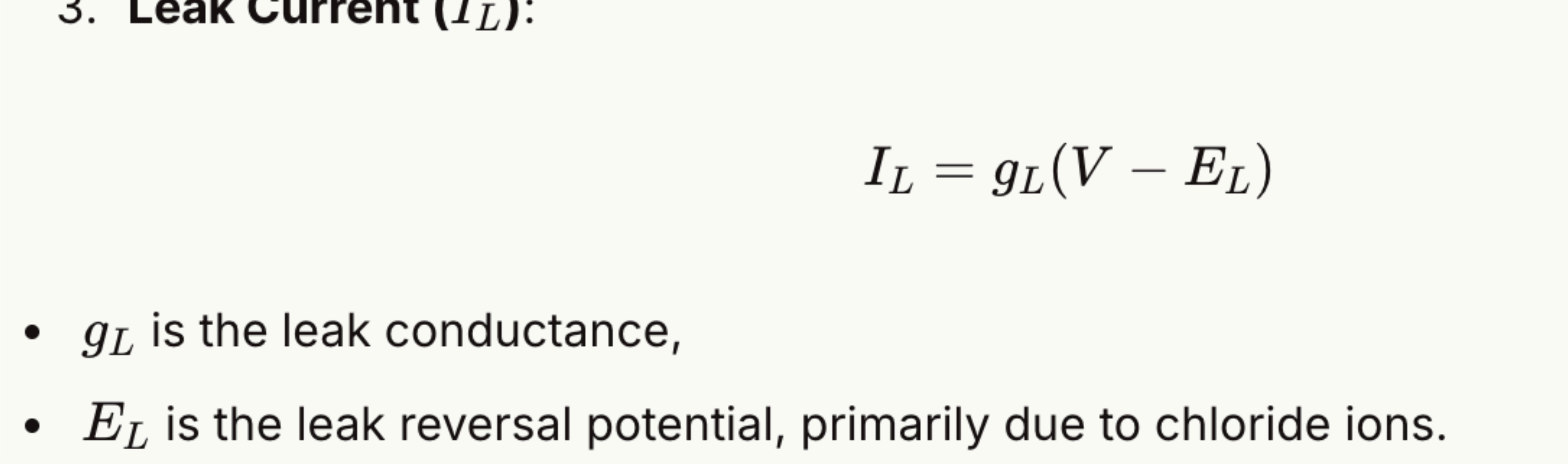
- $\overline{g}_{Na}$ is the maximum sodium conductance,
- m and h are gating variables representing activation and inactivation



2. **Potassium Current (I_K):**

$$I_K = \overline{g}_K n^4 (V - E_K)$$

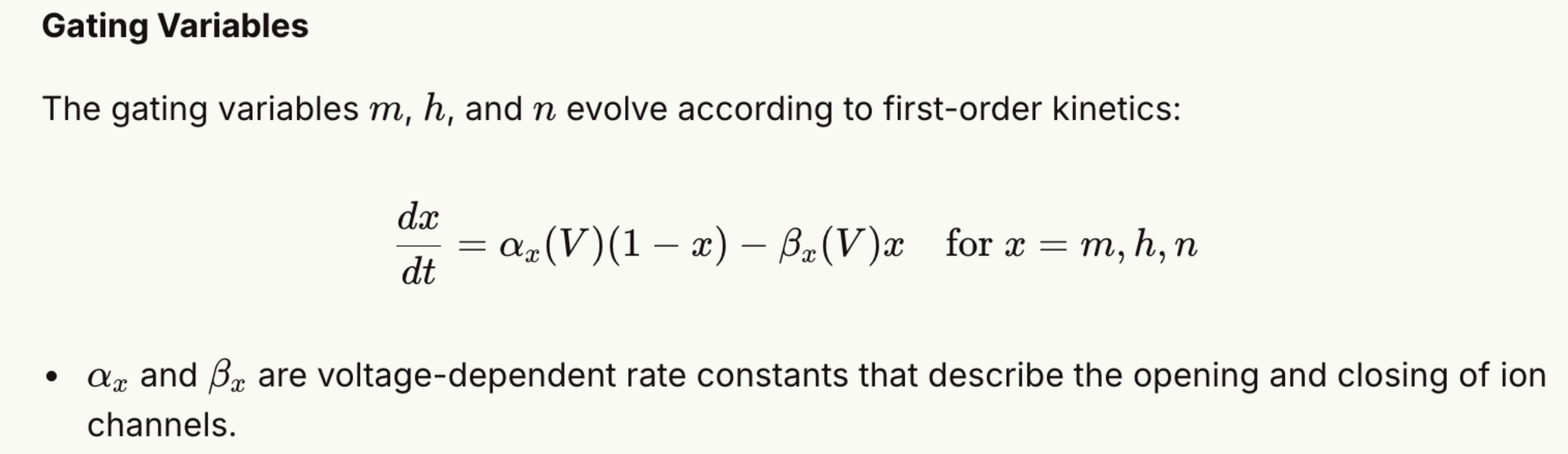
- $\overline{g}_K$ is the maximum potassium conductance,
- n is the activation gating variable,



3. **Leak Current (I_L):**

$$I_L = g_L (V - E_L)$$

- g_L is the leak conductance,
- E_L is the leak reversal potential, primarily due to chloride ions.



Gating Variables

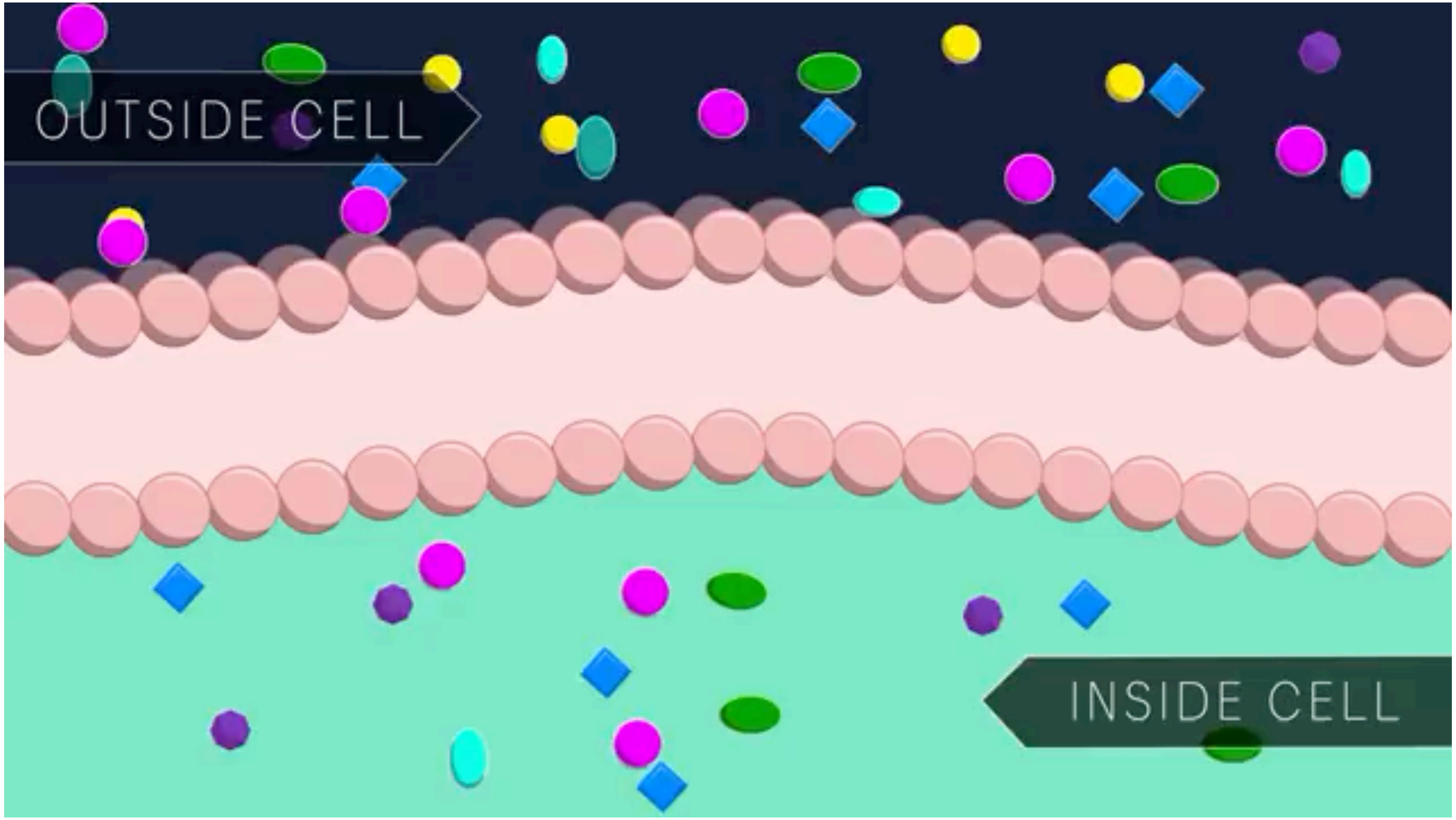
The gating variables m, h, and n evolve according to first-order kinetics:

$$\frac{dx}{dt} = \alpha_x(V)(1 - x) - \beta_x(V)x \quad \text{for } x = m, h, n$$

- α_x and β_x are voltage-dependent rate constants that describe the opening and closing of ion channels.

Implementation level models

Hodgkin and Huxley



Implementation level models

Hodgkin and Huxley

Description:

- Model of single-neuron spike generation, focusing on ion channels and action potentials.

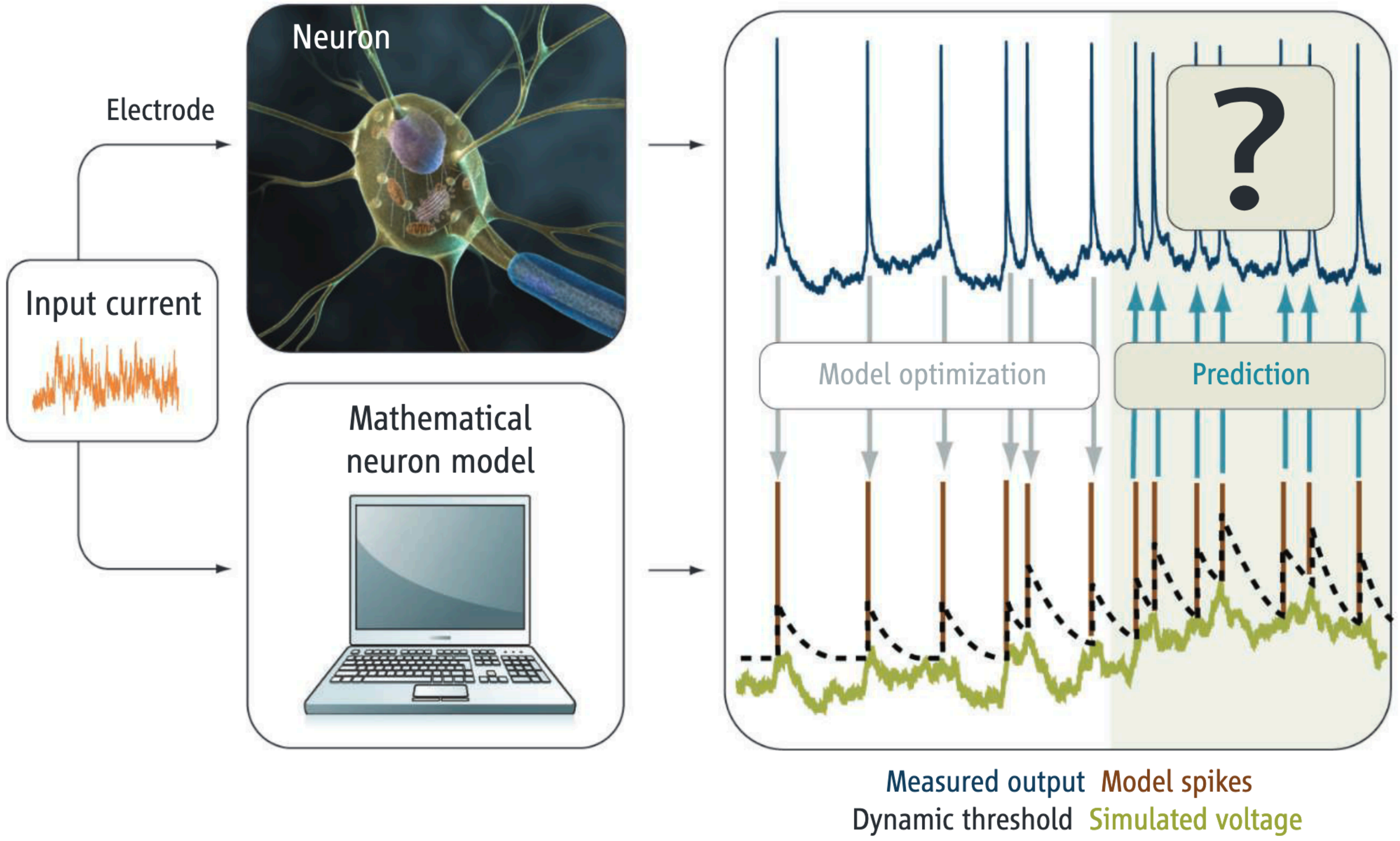
Advantages:

- Explains the mechanism of action potentials
- Synthesizes large amounts of neural data
- Describes latent variables (e.g., channel opening/closing, ion currents)
- Allows studying the effects of interventions (e.g., channel blockers)
- Enables real predictions (e.g., conditions for action potential onset

Limitations:

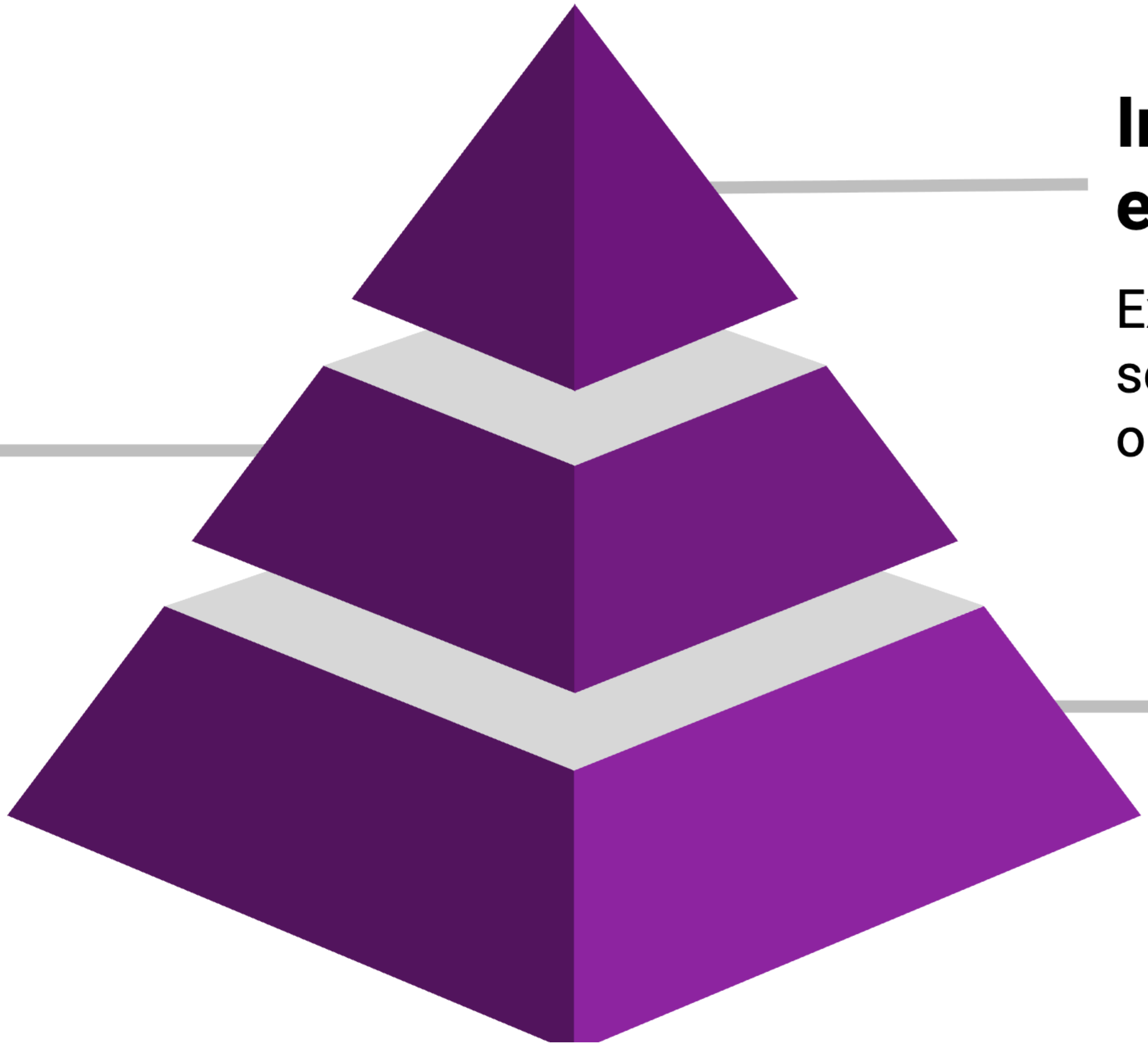
- Does not explain the molecular mechanism of ion channel opening/closing
- And?

What is a good neuron model?



International Neuroinformatics Coordinating Facility (INCF) launched
international competition (6) that allowed a quantitative comparison
models.

The model universe



Interpretive / explanatory - “why?”

Explain why the brain does something, e.g. because it’s optimal - **Tutorial 3**

Mechanistic - “how?”

Show how neural circuits perform complex function - **Tutorial 2**

Descriptive - “what?”

Compact summary of large amounts of data - **Tutorial 1**

Dayan & Abbott (2001)

https://compneuro.neuromatch.io/tutorials/W1D1_ModelTypes/student/W1D1_Intro.html

Further thougts on explanation in neuroscience

- Historically, computational neuroscience and psychology often treated computational explanations as autonomous from neural mechanisms (e.g., the "computational chauvinism" perspective). However, this autonomy is challenged by the difficulty in discovering neural implementations for high-level psychological theories when neural details are ignored.
- Computational chauvinism assumes that computational explanations in psychology are proprietary and do not require neuroscientific evidence. This perspective is problematic because it overlooks the need for mechanistic grounding—understanding how computations are physically realized in the brain. The author proposes that mechanistic models—those that explicitly link mechanisms to phenomena—are essential for meaningful computational explanations in neuroscience.
- Autonomous computational accounts (e.g., early AI models) often fail to map back to real neural mechanisms, limiting their explanatory power. The lack of integration between high-level computational theories and neural data has led to a pattern of failure in discovering implementations, undermining the strict division between computational and neuroscientific explanations.
- Computational explanations in neuroscience must ultimately be grounded in mechanisms to be fully explanatory. Neuroscience and computational modeling are interdependent: computational models need to align with neural data to avoid being mere abstractions. Empirical findings show that neural details are crucial for understanding cognitive processes, contradicting the idea that psychology can ignore neuroscience.

When Marr addresses the key explan tional model or algorithmic descripti under investigation, his position cha above, his general computational fram putation might be performed by any number of diverse hardwares. Yet, on nation of a particular cognitive capacit idea that any computationally adequ input-output transformation or com explanation of how the computation i the fact that after outlining their co crossings in early vision, Marr and H "whether the human visual system im to them" (Marr and Hildreth 1980 This is not an ancillary task. They c their explanatory account. For Marr, th human visual system (e.g., the re is crucial not only for building succe building successful explanations. Acco computational and algorithmic speci be assessed in terms of how well the details from neuroscience about their pany with computational chauvinists are autonomous and unconst