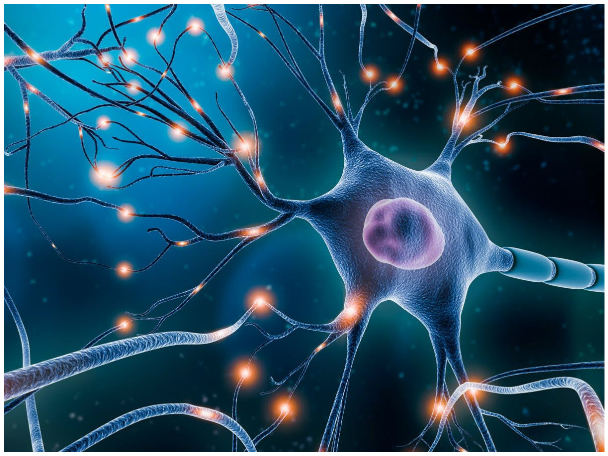
Neuromatics- How mathematics might solve the deep mysteries of Neuroscience



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Imagine you are running a marathon. Everytime you see a water stall, you stop for a break. How?

Now, think about your dog. When you throw that stick, it wags its tail and bullets in the direction of the throw. How?

Let's look at the common thread here: Living beings regulate motion based on visual stimulus. And it's not just regulation. Our ability to ensure that we don't clash into the pile of water bottles at the marathon or the dog catches the stick exactly at the right moment and position is quite extraordinary. Exactly how are we able to identify which speed and acceleration to run at to reach a certain spot in a given time frame?

In July 2023, a report submitted in *Cell Reports* by the neuroscientists Elie Adam, Taylor Johns and Mriganka Sur of the Massachusetts Institute of Technology conducted this experiment with a mouse and found some promising, yet unexpected results.

The mouse was made to run on a treadmill within a simulated environment that appeared to be a long hallway with occasional light posts. The mouse was trained to stop at the light posts and was given a small reward (some water) at each stop. It was expected that the mouse would show some neurological spike whenever it saw the light post after the training – but this didn't happen. In fact, it turns out that the observations provide experimental proof that our mind is constantly using calculus to determine the optimal motion at every second!

Our brain is a complicated organ. And perhaps its simulation by using neural networks is even more complex. But what better way to map out our brain's behavior than use math!!

Let's start with the Nernst Equation and the GHK Equation.

Both of these equations lie on the basic principle of the Nernst Potential.The two factors that most significantly affect the membrane potential are the electrostatic forces and the concentration gradients of each ion individually. But there's a small loophole in our theory so far. The resting potential of a cell (–70 mV) does not guarantee that the forces exerted by these two factors will lead up to a net of 0 N. The point at which this becomes true is called the nernst equilibrium and this potential itself is the nernst potential. Here's how it's calculated:

Now, let's try to see if this equation helps us connect some of the previous ideas. We know that Cl^- ions do not move across membranes. Apart from the fact that there just aren't enough leakage channels for Cl^-, this is because, when we calculate the nernst equilibrium for Cl^- ions using the equation above, we get a value very close to –70 mV, which coincidentally happens to be the neuron's resting potential as well. So at the resting potential, the Cl^- ions are at rest because the net force on them (from the electrostatic pull and concentration gradient) is almost 0 N.

Great! Now we know how to find the exact point when the net ion flow will be null in a neuron. Or do we?

The Nernst Equilibrium applies only for one particular ion that you chose to consider. That is to say, even though the Na^+ ions may have achieved a nernst equilibrium at, say x mV, the other ions have not. So, these ions continue to transfer charge and therefore manage to disturb this voltage every nanosecond. So our job now, is to look for a certain point when all, and not just one, ions are at rest. This point will not necessarily be the point of equilibrium for a specific ion but will rather be a steady state for all ions at once.

Obviously, one such point is –70 mV. But is this the only point? What if we were to magically tweak the overall concentrations of ions in a neuron? How would we know the steady state then?

The answer is simple: The GHK Equation. Here's how it looks:

$$V = \frac{RT}{F} ln\left(\frac{P_K[K]_{out} + P_{Na}[Na]_{out} + P_{Cl}[Cl]_{in}}{P_K[K]_{in} + P_{Na}[Na]_{in} + P_{Cl}[Cl]_{out}}\right)$$

$$R = 8.314,\ F = 96485,\ T = temp\ in\ Kelvin,\ P_{ion} = permeability\ of\ ion,$$
$$[ion]_{in} = conc.\ in\ cell,\ [ion]_{out} = conc.\ outside\ cell$$

Note that in this equation, we are only considering K+, Na+ and Cl– ions because these three take up more than 95% of the fluid composition inside and outside a neuron. Also, if we need to find the force with which a particular type of ion will move (the driving force), all we need to do is subtract its nernst equilibrium from the GHK value. While the answer we get is not actually a force per se, it will be enough to give the direction of ion flow.

Now, let's take a look at two important constants which will help us determine the effect of resistance and capacitance upon the voltage transmitted through the axon hillock: the length constant and the time constant.

$$Length\ constant\ (\lambda) = \sqrt{\frac{R_{membrane}}{R_{axial}}}\ \ \&\ \ Time\ constant\ (\tau) = R_{membrane} C_{membrane}$$

Length constant (λ) — Given in the unit metres, every time the length constant distance is covered, the voltage value reduces to 36% of its original value

Time constant (τ) — Given in the unit seconds, every time the time constant time is covered, the voltage value is reduced by 64% of its original value

There are also many other equations which can be used for understanding the chemical processes involved in the perception of signals within the human brain, some of which are shown below.

Nernst Equation

$$E_{ion} = \frac{RT}{zF} ln \frac{[ion]_o}{[ion]_i}$$

for T in Kelvin, R = 8.314 *J/K*mol*, and F = 96, 485 *C/mol*

ln = natural log, base e (~2.718)

GHK Equation

$$Vm = \frac{RT}{F} ln \frac{P_k[K]_o + P_{Na}[Na]_o + P_{Cl}[Cl]_i}{P_k[K]_i + P_{Na}[Na]_i + P_{Cl}[Cl]_o}$$

for T in Kelvin, R = 8.314 *J/K*mol*, and F = 96, 485 *C/mol*

Driving Force

$$Driving\ Force = V_{membrane} - E_{ion}$$

Ohms Law

$$Current\ (I) = \frac{Voltage\ (V)}{Resistance\ (R)}$$

Current in Amps (*A*), Voltage in Volts (*V*), Resistance in Ohms (*Ω*)

Length Constant

$$Length\ Constant\ (\lambda) = \sqrt{\frac{R_{membrane}}{R_{axial}}}$$

$R_{membrane}$ in *Ω*cm*, R_{axial} in *Ω/cm*

Time Constant

$$Time\ Constant\ (\tau) = R_{membrane}C_{membrane}$$

$R_{membrane}$ in Ω*cm, $C_{membrane}$ in F

Obviously, that's not all–the breadth and depth of neuroscience is way beyond the surface details we have covered. It's always surprising and fascinating how a life science such as biology is so closely intertwined to both chemistry and mathematics in such a subtle and beautiful way. What's more intriguing is the fact that neuroscience forms the basis of a technology that is arguably one of the booming fields in our world.

With closer simulations of how the mind works, the prospects of creating a similar neural network are increasing and it's just a matter of time before we reach the proficiency to create full-sized human bots!