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Wisdom of (molecular) crowds: How a snake's temperature-sensing superpower separates information from misinformation

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The namesake pit organ of pit vipers and other temperature-sensing snakes is a remarkable biological thermometer, one that converts infrared light into an electrical signal (Bullock and Diecke 1956). The organ is arranged like a pinhole camera, with a small outward-facing opening covering a pit membrane dense with neuronal projections. This geometry ensures that only light from a narrow angular cone lands on the membrane. By reorienting its head to scan its surroundings, the snake can precisely detect and localise warm-blooded prey even in complete darkness.

The molecular mechanism that underlies the pit membrane's infrared-sensing capacity has been worked out. Long-wavelength photons heat biological tissues by exciting a variety of non-specific molecular vibrational and rotational states. Unlike visible-light photons, which are directly sensed in photoreceptors via the specific photochemical activation of rhodopsin (Rieke and Baylor 1998), infrared photons are indirectly sensed in pit membrane neurons via the non-specific thermal activation of TRPA1 ion channels (Gracheva *et al.* 2010). In its open state, this channel creates an inward cation current that depolarises the cell membrane and triggers an action potential. As temperature increases, so does the opening probability of the channel, leading to a higher neuronal firing rate.

While individual TRPA1 dynamics account for the qualitative features of the system, a central quantitative mystery remains. In both the visual and infrared-sensing systems, receptors can be spontaneously activated in the absence of incoming photons, due to the ambient temperature. How is this spontaneous noise separated from the actual signal caused by photon absorption? In the visual system, rhodopsins have evolved an extremely low thermal activation rate to enable dim-light sensing (Rieke and Baylor 1998). In the infrared-sensing system, TRPA1 channels have evolved a sharp variation in opening probability, going from near 0 to near 1 across a 1 K variation in temperature (Gracheva *et al.* 2010). However, even this level of sensitivity in TRPA1 channels is not sufficient to explain how individual neurons can detect the milli-Kelvin variations in temperature needed to detect prey (Bullock and Diecke 1956). Neurons are evidently able to sense parts-per-thousand variations in channel opening probability. How is this achieved? In a recent paper, Graf and Machta (2024) propose an elegant solution to this mystery.

In their 1977 classic, 'Physics of chemoreception', Howard Berg and Edward Purcell explained how information from noisy molecular reporters could be combined to produce a reliable signal (Berg and Purcell 1977). The key is to perform repeated measurements across a large number of molecules. Suppose we have N channels in the neuron. We can get uncorrelated snapshots of each channel at time intervals τ_C, and we have a total time τ_{tot} to make the measurement. Let us assume that the channel opening probability $p(T)$ is linear about the midpoint temperature T_0, going from fully closed at $T_0 - 0.5$ K to fully open at $T_0 + 0.5$ K. For a 1 mK increase from the midpoint temperature T_0, the opening probability of a single channel goes from $p = 0.500$ to $p = 0.501$. The number of times we see a channel open is like a coin toss, binomially distributed with probability p over $N_{tot} = N\tau_{tot}/\tau_C$ independent trials. To distinguishing a fair coin ($p = 0.500$) from one with a very small bias ($p = 0.501$), the standard deviation $\sqrt{N_{tot}}/2$ should be smaller than the difference of the means $N_{tot}/1000$, so $N_{tot} > 2.5 \times 10^5$. Plugging in plausible values of $N = 10^5$ receptors, $\tau_C = 10\,\text{ms}$ and $\tau_{tot} = 100\,\text{ms}$ (Graf and Machta 2024), we find $N_{tot} = 10^6 > 2.5 \times 10^5$. That is, there are indeed enough channels in each neuron and enough measurements per channel during the available time window to detect the effect of a milli-Kelvin variation in temperature.

How is this complex operation, combining information across time and ion channels, actually carried out in practice? We can get intuition from what appears to be an unlikely quarter: the spread of gossip. Understanding the flow of information and mis-information across social networks has grown into an active area of research (Lazer *et al.* 2018), with profound implications for collective decision-making in modern societies. For example, election campaigns are beset with false claims, and individual citizens must somehow separate truth from falsehood when deciding whom to vote for. The snake faces a very similar challenge in distinguishing the spontaneous thermal activation of individual channels (noise) from a systematic infrared photon-induced activation (signal), corresponding to the presence of prey. We can make this analogy precise.

Consider a perennial topic of gossip, the rumour that actor X is the next James Bond. Should we believe it? While there may be a few people who know the actual facts, most people who share this rumour on social media will do so based on the chatter that already exists. This is a type of positive feedback, captured by figure 1 (adapted from Gracheva *et al.* 2010):

We imagine a population of N individuals who can share posts on social media (brown gossip nodes, figure 1A). In addition, there are T individuals who are reliable sources of information (green truth nodes, figure 1A). Importantly, each gossiping individual does not know whether what they are reading is reliable or not (that is, they do not know whether the incoming arrow is green or brown). The level of gossip is captured by the number of recent gossip posts on the James Bond topic (x-axis, figure 1B, C). The probability that an individual shares a post they have read, thus creating more gossip, is a rising function of the existing level of gossip (blue sigmoidal curve, figure 1B). If the number of truth nodes increases from T to $T + \Delta T$, true posts will supplement the gossip posts, and so the blue curve will shift to the left (a higher chance of sharing for the same level of gossip, figure 1C).

However, there is a countervailing force at work: gossip thrives on novelty, so old posts are ignored. This can be captured by assuming each post has a finite lifetime, and so the total removal rate is proportional to the total number of existing posts (purple line, figure 1B). The net change in the level of gossip corresponds to the difference between the creation and removal rates: gossip will increase whenever the blue curve is above the purple line (brown rightward arrows, figure 1B). We now add an important ingredient: we assume that mainstream reporters are monitoring the gossip, and will publish a news report (‘Actor X is the next James Bond’) once the level of gossip crosses some threshold (blue dashed vertical line, figure 1B). As soon as this happens, the story is no longer deemed gossip-worthy, and the overall level of gossip on this topic resets to zero (figure 1B).

If the blue sigmoidal curve is sufficiently steep, it will intersect the purple curve at three points (figure 1B, C; figure 2). The leftmost and rightmost points (filled circles) are low and high steady-state levels of gossip: if you start near these points, you will tend to stay there. The middle point (empty circle) is an unstable separator point: start to the left, and the level of gossip drops to low; start to the right, and the level of gossip surges to high before

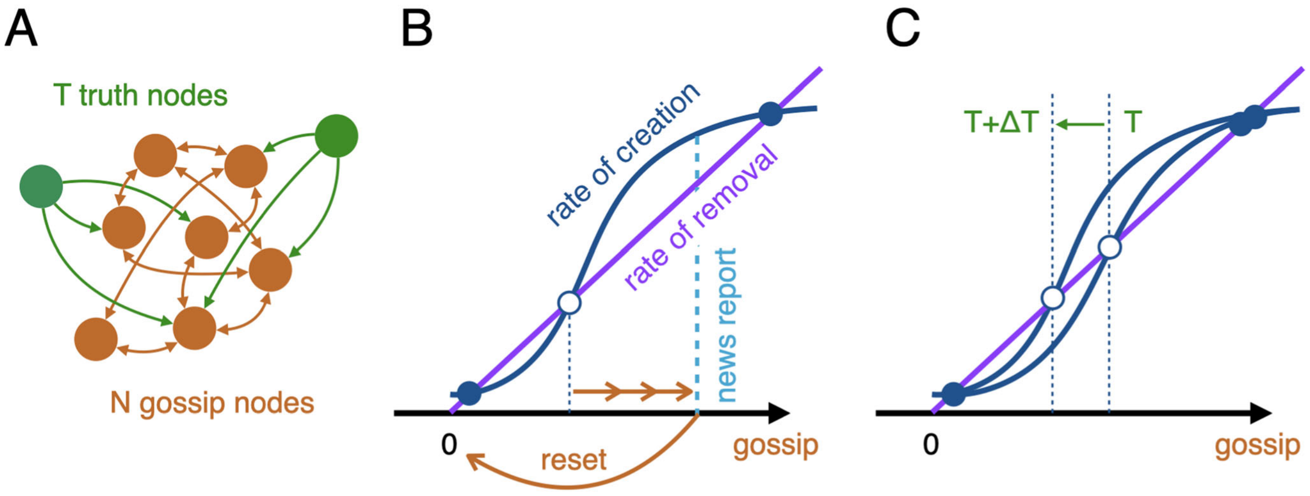

Figure 1. The spread of gossip in a social network.

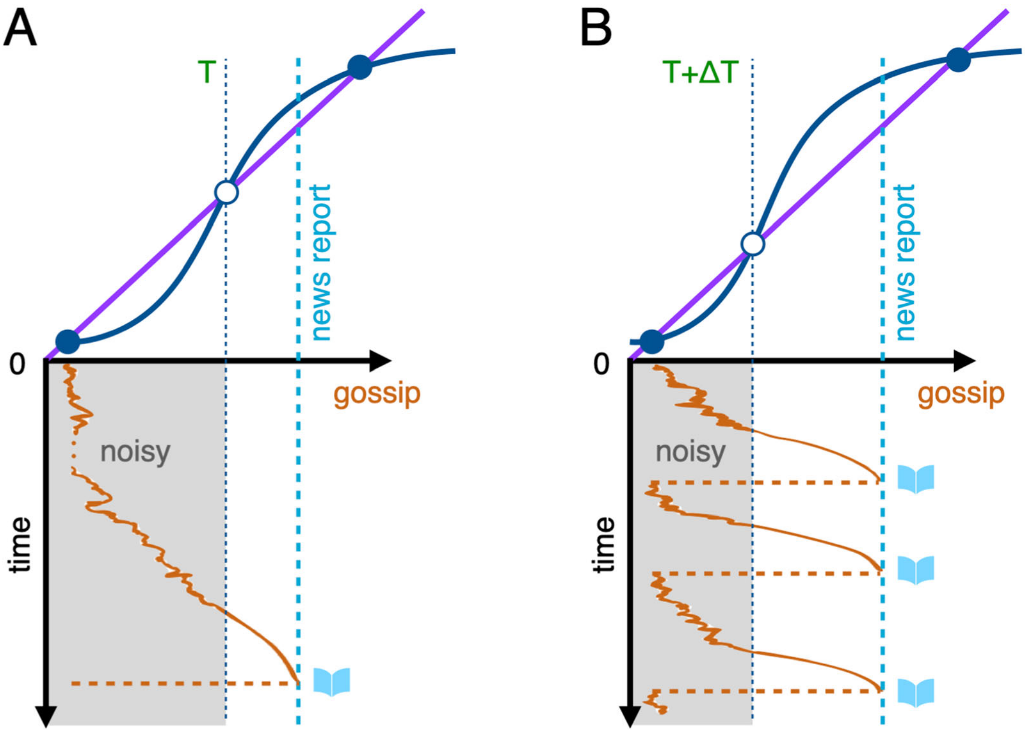

Figure 2. Noise-driven transitions from low-gossip to high-gossip states.

resetting. At least, this would be the deterministic expectation. However, the behaviour of individuals is stochastic: each makes a random choice to share a post or not. This means that even in the regime where we expect gossip to drop deterministically, there will be noisy fluctuations in gossip levels (gray zone, figure 2). Occasionally, these fluctuations can actually cross the separator point and then drive the system to a high-gossip state, leading to a news report (blue book icon). This is analogous to noise-driven transitions in other bistable systems such as gene networks or ecological systems (Assaf *et al.* 2013). The closer the separator point to the low state, the more often such a noise-driven transition will occur. Although news reports are rare overall, their frequency at $T + \Delta T$ will be much higher than at T (compare right and left panels of figure 2). In other words, your belief that 'actor X is the next James Bond' should be bolstered if news stories to this effect are relatively rare, but appear more often than they used to.

What does this mean for the snake's pit organ? A set of N interacting TRPA1 channels in a single neuron corresponds to the social network. The membrane potential (V) corresponds to the level of gossip (G). When one channel opens, it depolarises the membrane, raising V and increasing the probability that other channels will also open. The temperature (T) is the level of the incoming true signal. A single channel may open due to spontaneous thermal activation (pure gossip, the noise) or due to an incoming photon (true input, the signal), as captured by the blue curve in figure 1. In the absence of TRPA1 activity, the membrane potential returns to a resting level due to the activity of various membrane transporters and channels (mainly the Na^+–K^+ pump and K^+ channels). This is captured by the purple line in figure 1. The potential will increase whenever the blue curve is above the purple line. When the potential reaches a specific threshold (blue dashed vertical line) an action potential is fired, corresponding to a news report. The membrane potential then resets to the resting state. Exactly as we have seen in the gossip example, the frequency of action potentials in such a system is dependent on the temperature.

Graf and Machta (2024) show that the proposed TRPA1 dynamics can indeed achieve the observed hypersensitivity to temperature changes, but only if parameters are correctly tuned. If the blue curve is too far to the right, the frequency of action potentials is too low to make a rapid judgement; too far to the left, and the frequency does not vary much with temperature. The manner in which the stochastic activation of individual channels collectively drives the neuron to fire an action potential recapitulates the Berg–Purcell procedure, integrating information across channels and across repeated measurements over time. The authors show that information about the stimulus is proportional to the number of action potentials, but the absolute value of information per spike depends on how erratic the spikes actually are. By fitting their model to measurements of temperature-dependent spike frequency, the authors infer required values for the number N of TRPA1 channels and their decorrelation times τ_C to make the procedure effective. These predictions may be verified by future experiments.

The model of infrared detection presented here deals with computation happening *within* a single neuron. Further computations can be performed by integrating information *across* thousands of neurons in the pit membrane, over both space and time. While individual neurons have excellent thermal sensitivity, the pit organ as a whole appears to have low spatial resolution (Clark *et al.* 2022). Behavioural experiments suggest that snakes use rapidly changing thermal stimuli as the cue to localise prey, comparing measurements across time before striking (Schraft *et al.* 2019).

We have used the gossip analogy to understand the capacity of a neuron to separate signal from noise. But perhaps this connection could be reversed. The ability to separate friend from foe in an ecosystem, or self from non-self in immunity, is central to evolutionary fitness and expected to be highly optimised. It is possible that living systems have arrived at novel means of separating signal from noise in collective systems, which may inspire new algorithms to enhance the reliability of information flow in social networks.

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