



**From Neurons to Behaviour:  
Exciting Insights from the  
*Xenopus* Tadpole**

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Dr Kara Pratt

# FROM NEURONS TO BEHAVIOUR: EXCITING INSIGHTS FROM THE *XENOPUS* TADPOLE

Understanding how neurons come together and form circuits in the brain is crucial to understanding how the brain works. **Dr Kara Pratt** and her team at the University of Wyoming are uncovering the mysteries behind the formation of neural circuitry and the ability of neurons to self-organise into highly refined networks. An incredibly elegant series of experiments using the larva stage of frogs has progressed insight into this fundamental phenomenon of neuroscience, specifically in the visual system.

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## Neurons: The Puzzle Pieces of the Brain

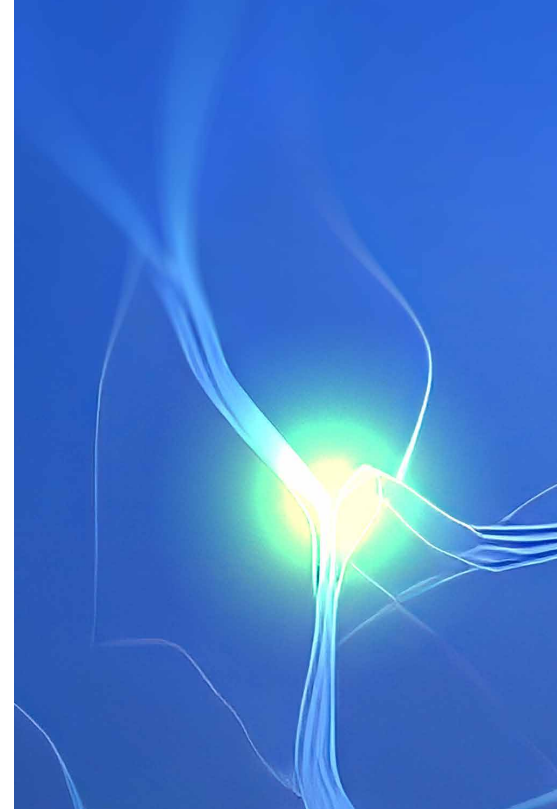
Neurons are the basic building blocks of the nervous system in the brain. They self-organise into circuits that allow correct brain functioning and information processing that ranges from basic sensory perception to complex cognitive processes. Imagine you have puzzle pieces, and you want to understand how they come together and form the puzzle image. In the world of neuroscience, this is a pivotal challenge, in which neurons are puzzle pieces that self-organise to form neural circuits. This question is crucial for a better understanding of the development of the brain and related processes.

Many psychiatric and neurological disorders are linked to problems in neural circuitry. Therefore, understanding neuronal assembly into neural circuitry is crucial not only for understanding how a healthy brain develops and functions throughout life but also for deeper insights when something goes wrong.

## The Tiny Brain Wonders of *Xenopus* Tadpoles

There are various methodologies that scientists use to delve into the intricate world of neural circuitry and the neuronal ability to self-assemble. One captivating model to unveil these phenomena is the *Xenopus* tadpole, which is the larva stage of a frog. It provides an important scientific model allowing us to unravel the intricacies of how tadpoles transmit information from their eyes to their brains, and how these connections help them react to objects and events.

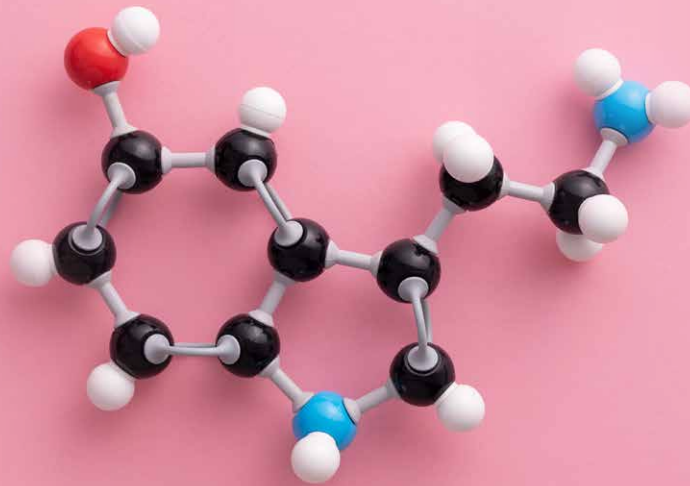
Leading the charge in this fascinating area are Dr Kara Pratt and her dedicated team at the University of Wyoming. They are especially interested in advancing the knowledge of the molecular pathways that underlie the process of neuronal self-organisation into highly refined, functionally distinct networks. More specifically, their work elucidates how different components of the visual system are involved in processing different aspects of the visual scene, and how this visual information consequently impacts behaviour.



These vital insights are gleaned from recording the electrical activity of individual neurons in the developing visual systems of *Xenopus* tadpoles and, alongside this, studying the visual system at the behavioural level. This combined approach provides a particularly powerful model with which to understand how neural circuits form and give rise to behaviours.

## Studying Visually Guided Behaviours

As a postdoctoral researcher in Dr Carlos Aizenman's laboratory at Brown University, Dr Pratt was part of the team that identified an exciting new behaviour in tadpoles. A novel behavioural assay known as a 'moving dot test' allowed the team to [characterise visual avoidance behaviour](#) in the laboratory, that is, when tadpoles swim away from specific visual stimuli. In the wild, this often occurs in potentially dangerous situations and evolved as a survival mechanism. The moving dot test takes advantage of the observation that tadpoles will usually dodge moving dots projected onto the floor of their test dish. These moving dots serve as visual cues that tadpoles respond to by swimming



## serotonin

away. Dr Pratt is now working to explain how the visual system in tadpoles transforms such visual (i.e., sensory) input into motor output (i.e., behaviour).

### From Seeing to Avoiding to Attraction

In a state-of-the-art review, Dr Pratt's team summarised the existing literature on the topic of visual avoidance behaviour, pointing to the critical role of the tadpole retinotectal circuit in visual avoidance behaviour. This circuit is made up of special cells in their eyes that send the message to the optic tectum, the part of the amphibian brain that processes visual stimuli. A properly formed and refined retinotectal projection is essential for visual-avoidance behaviour, and it is thus unsurprising that it develops quickly in young tadpoles, with immature connections between the eye and tectum forming within days of fertilisation, maximising their chances of survival.

With the help of research students in her team, Dr Pratt set up a novel experimental design to answer two key questions. The first one was whether there were any other visually guided behaviours in tadpoles. If so, the second question was to find out whether those were also related to the retinotectal projection system – or some other component of the circuit.

In an important departure from previous research, the team investigated whether there was a visual stimulus that the tadpoles would swim towards (i.e., a stimulus that they would be attracted to rather than one they would avoid). They achieved this using a [novel visual preference paradigm](#) to measure the long-term preferences of freely swimming tadpoles.

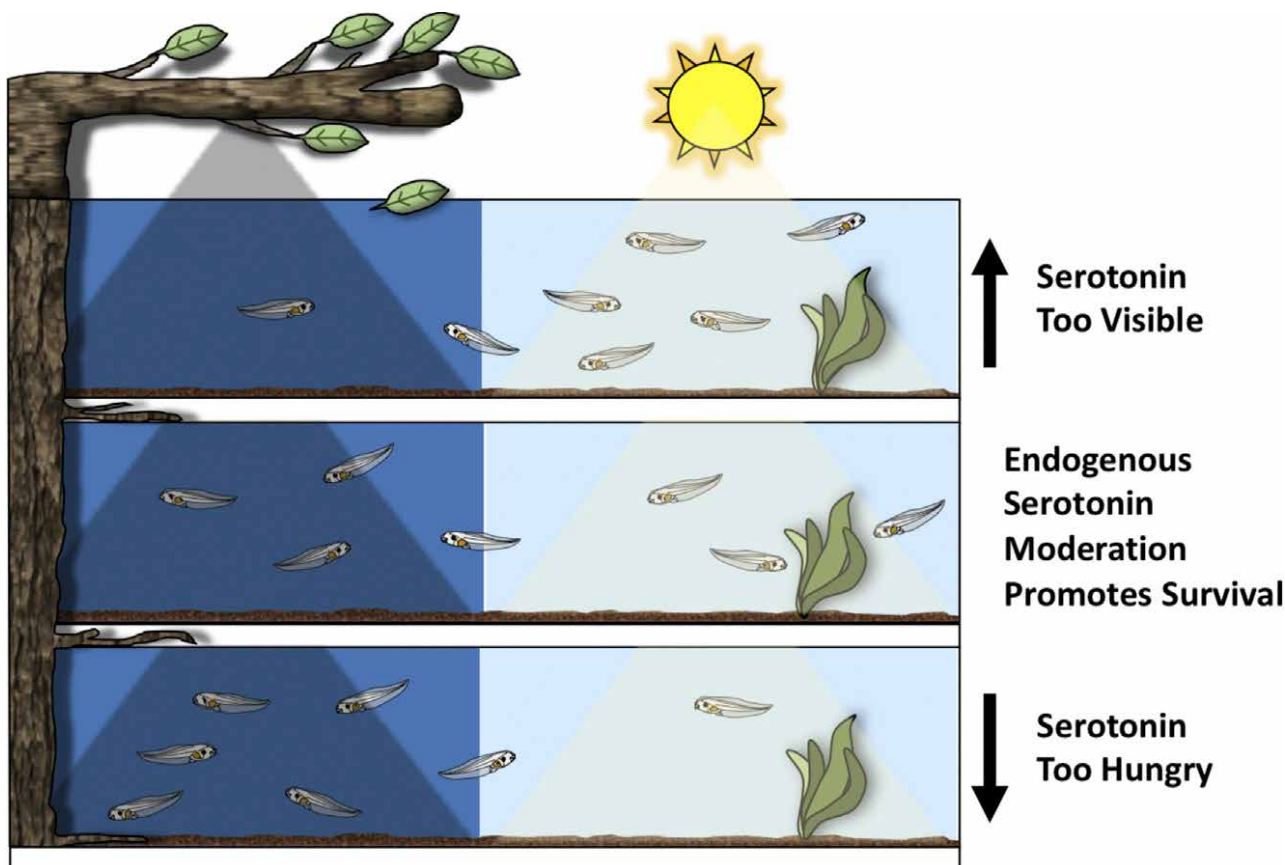
### Tadpoles Prefer the Colour Green (But How?)

This novel experiment showed, for the first time, that tadpoles prefer the colour green – in other words, they spent most of their time in the green area of the test dish. They preferred green when green was pitted against light, and they preferred green when green was pitted against dark.

Bearing in mind that the entire visual system comprises many distinct circuits, Dr Pratt was keen to identify which circuit(s) of the visual system are required for this behaviour in the tadpoles to take place. To this end, the team surgically removed different parts of the circuit and repeated the experiments. This revealed that the midbrain tegmentum (part of the visual processing centre) was critical, whereas the optic tectum, another visual processing centre, was not required for the tadpoles to display the innate preference for green. Notably, in humans, Dr Pratt notes that this brain area is also involved in different movement and motivation functions.

But how is it that tadpoles prefer the colour green? In other words, how is this preference for green manifested? The team determined that the preference for green is manifested by tadpoles slowing down, oftentimes even stalling, when they are in the green region of the test dish. Thus, for tadpoles, green means 'stop!'.

Dr Pratt suggests that this could be caused by the neurotransmitter serotonin (a brain molecule that regulates various physiological and psychological processes in the body). Her premise is based on research from [Professor Nick Spitzer's](#) laboratory, revealing that increased levels of serotonin result in shorter swimming bouts. Dr Pratt and her team suspected that changes in serotonin levels may influence tadpoles' preference for the colour green, too.



Credit: Harley Yerdon

To test this, the researchers exposed tadpoles to selective serotonin reuptake inhibitors (SSRIs) for 24 hours. These drugs are used to control levels of serotonin in depression, for example. To Dr Pratt's surprise, the SSRIs did not increase the existing preference for green. Regardless of the experimental manipulation, tadpoles consistently preferred the brightest part of the dish. This gave the researchers a new and intriguing idea – the SSRIs shifted the preference from colour-based to luminance-based.

### Serotonin's Role in Tadpoles' Visual Preference

These latest findings and possibilities spurred the team to explore the visual preference of tadpoles further. In the next series of experiments, the team switched to a simpler design of 'light versus dark' to test only the preference for luminance. The results were fascinating! The study showed that the tadpoles' preference for luminance peaks at around 4 pm and is lowest at night. When the team used the SSRIs to enhance levels of serotonin transmission, the preference for light increased significantly. However, when serotonin levels were decreased by exposing tadpoles to an inhibitor of tryptophan hydroxylase (an enzyme that synthesises serotonin), the preference for light decreased, too. This strongly suggests that serotonin, the naturally occurring chemical in the brain, creates the preference for light over dark in *Xenopus* tadpoles.

### Putting Together the Pieces

Dr Pratt has advanced insights into the visual preferences of tadpoles, and how these preferences take place. First, her work

shows that normally, tadpoles display a modest yet significant preference for green over light, and also a preference for light over dark. Second, she has shown that artificially enhancing the level of serotonin transmission leads to an abnormally strong preference for light. Finally, we now know that inhibiting serotonin levels in tadpoles significantly reduces the preference for light.

These patterns likely reflect survival mechanisms. Dr Pratt and the team theorise that spending time in well-lit regions during the day may be important in order to find food or to dwell near sun-warmed regions of water. Similarly, it may be important for them to spend time near green plants that are a source of food and safety. This preference, which is neither too strong nor too weak, may be optimal for their survival according to so-called predator-prey interactions theories. These models suggest that being too predictable in behaviour could make tadpoles more vulnerable to predators.

Having established the importance of the maintenance and timely release of the optimal levels of serotonin during the day, Dr Pratt's work highlights that naturally occurring brain chemicals such as serotonin may play a crucial role in shaping how neural circuits form and function. She is now investigating the underlying neural circuits that give rise to these visual preference behaviours and, importantly, how serotonin modulates these circuits.



# Meet the Researcher

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Dr Kara Pratt received her PhD in Neuroscience from Brandeis University in 2004. After undertaking several postdoctoral positions at Brown University, the University of Washington, and Massachusetts General Hospital, she started her own laboratory at the University of Wyoming. She has worked as an Assistant Professor in the Department of Zoology and Physiology since 2011 and was promoted to Associate Professor in 2017. Dr Pratt is specifically interested in researching the molecular pathways underlying the developing visual systems of the *Xenopus* tadpole. She has been supported by prestigious funding and has published over 28 peer-reviewed journal articles to date. On top of her research endeavours, she teaches courses in neurodevelopmental and developmental biology.

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### FURTHER READING

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