# Short introduction to the project. Neuronal pathfinding

## Next steps and improvements:

1. ~~Add the references~~
2. ~~Translate the thesis paragraph to what you want to do and why~~ **~~(1) Extension to the optic fiber layer~~**
   1. **~~Formulate clear tasks to be accomplished by your model~~**
   2. **~~Include assumptions~~**
   3. **~~Include objectives – chemoattractors, chemorepellents~~**
   4. **~~Include potential problems~~**
3. ~~Include abbreviations – didn’t need that, only RGC used~~
4. ~~List of all molecules and if they are repellent or attractive~~ (include source?)

## Key facts that need to be covered:

1. Neurons – basic components – cell body and axon
2. Axons have specific places they need to go to to connect
3. How do axons know where to go? – chemical guidance
4. Inspiration – the optic pathway
5. Example molecules:
   1. Chemoattractors
   2. Chemorepellents

## First draft:

One complex problem in neuroscience is how the nervous system is formed. In the brain neurons form complex structures that have very specific connections. Neurons have cell bodies that do signal processing, dendrites which accept input and axons that extend to form connections to other neurons in specific areas. The question is how axons know in which direction to grow and where to go to connect to the correct downstream neurons.

One biological model used to explore this question is the optic pathway. During embryonic development the tissue that becomes your brain is folded in such a way that some of it ends up in your eyes – that is the neural retina. The neurons that form this tissue are called retinal ganglion cells (RGC). They end up separated from the rest of your brain and need to send their axons back to the brain so you can see. The path they take is complex with multiple decision points (but only one type of neuron) which makes it perfect for exploring axon guidance.

RGC axons grow through multiple decision points. They (1) grow to the optic fibre layer at the inner surface of the retina, (2) extend to the optic disc, (3) exit the eye, (4) grow to the optic chiasm where, in species with binocular vision, they chose to either project contralaterally crossing the ventral midline of the brain or project ipsilaterally, and finally, (5) reach the primary visual centres of the brain – superior colliculus and lateral geniculate nucleus in mammals (Herrera, Erskine and Morenilla-Palao, 2019).

A diagram of the internal organs

AI-generated content may be incorrect.

**Figure 1. Optic pathway (mouse).** Retinal ganglion cell axons travel from the retina, through the optic disc, via the optic nerve, to the optic chiasm. There, they continue either contra or ipsilaterally to the optic tract and the higher visual centers. Taken from Erskine and Herrera (2014).

It would be amazing to make a full model but that is a little ambitious so let’s start with the first step of this journey.

Diagram of a diagram showing the structure of the veins

AI-generated content may be incorrect.

Kwon, Y.H. *et al.* (2009) ‘Primary open-angle glaucoma’, *New England Journal of Medicine*, 360(11), pp. 1113–1124. doi:10.1056/nejmra0804630.

Diagram of a human eye anatomy

AI-generated content may be incorrect.

<https://gene.vision/retina/>

**Extension to the optic fiber layer**

The first step in RGC axon pathfinding is extension to the optic (retinal nerve) fiber layer. This is achieved via combination of repulsive signalling from the inner retina and the attractive properties of the optic fiber layer. Some of the factors that we know guide axons are **NCAMs** – neural cell adhesion molecules which attract axons to the optic fiber layer (Halfter *et al.*, 1987; Brittis *et al.*, 1995) and **slits** secreted from the cells of the inner retina – which repel the RGC axons (Thompson *et al.*, 2006, 2009).

(Other molecules)

Model info:

Slits (Slit 1 and Slit 2) – repel RGC axons – secreted by amacrine cells (interneurons)

Amacrine cells – size – small field 7-10 µm – distance bw them 20 - 50 µm (center to center)

Large field 7-15 µm - distance bw them 100 - 150 µm (center to center)

Large field mainly involved in slits.

NCAMs secreted by RGC axons – makes sense to make a tract

Muller glia – secrete laminin - repel

Model strategy:

Focus on slit signalling to guide away from inner retina:

A diagram of cell layers

AI-generated content may be incorrect.

**Assumptions:**

Amacrine cells in place secrete slit – which repels RGCs

**Objective:**

Place random amacrine cells which secrete slit

Need to figure out how to program repulsive gradient

Place RGC(s) – guide away

Introduce random noise?