

Too much 'noise' can affect brain development

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Using cutting-edge imaging technology, University of California, Irvine biologists have determined that uncontrolled fluctuations (known as "noise") in the concentration of the vitamin A derivative Retinoic acid (RA) can lead to disruptions in brain organization during development.

Identifying how a cell responds to a signal made by another cell, despite the level of [noise](#) present, may improve our understanding of [developmental disorders](#).

Thomas F. Schilling, professor of developmental & cell biology, and his colleagues, published this study online at *eLife*.

During development, RA is an important secreted molecule that aids in the proper organization of the brain. The cellular response to RA depends upon its concentration, which is determined by its production, movement through tissue and interactions with many proteins within the cell. During normal development, cells can filter the "noise" in RA levels and establish appropriate [brain organization](#). Schilling and study lead author Julian Sosnik wanted to measure the fluctuations in RA and determine how cells respond to the proper amount despite the presence of constant noise.

To accomplish this, they used fluorescence lifetime imaging to exploit the auto-fluorescent nature of RA and measure its distribution across the developing zebrafish embryo. The team found that RA forms a gradient in the embryo, with a lower [concentration](#) at the head. They also

observed that a large amount of noise exists within the RA gradient.

They identified one protein within developing cells that interacts with RA to help reduce the noise. When this protein was altered, cells could no longer control the level of noise within the RA gradient, which led to [disruptions](#) in brain organization.

With this, the researchers concluded that noise reduction within cells is critical for the proper response to the RA gradient and normal organization of the brain.

Future studies will employ new transgenic technologies to examine levels of noise in the expression of genes responding to RA in developing brain cells and address potential beneficial roles for noise in helping switch cells from one type to another in this system.

More information: Julian Sosnik et al. Noise modulation in retinoic acid signaling sharpens segmental boundaries of gene expression in the embryonic zebrafish hindbrain, *eLife* (2016). [DOI: 10.7554/eLife.14034](https://doi.org/10.7554/eLife.14034)

Provided by University of California, Irvine

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