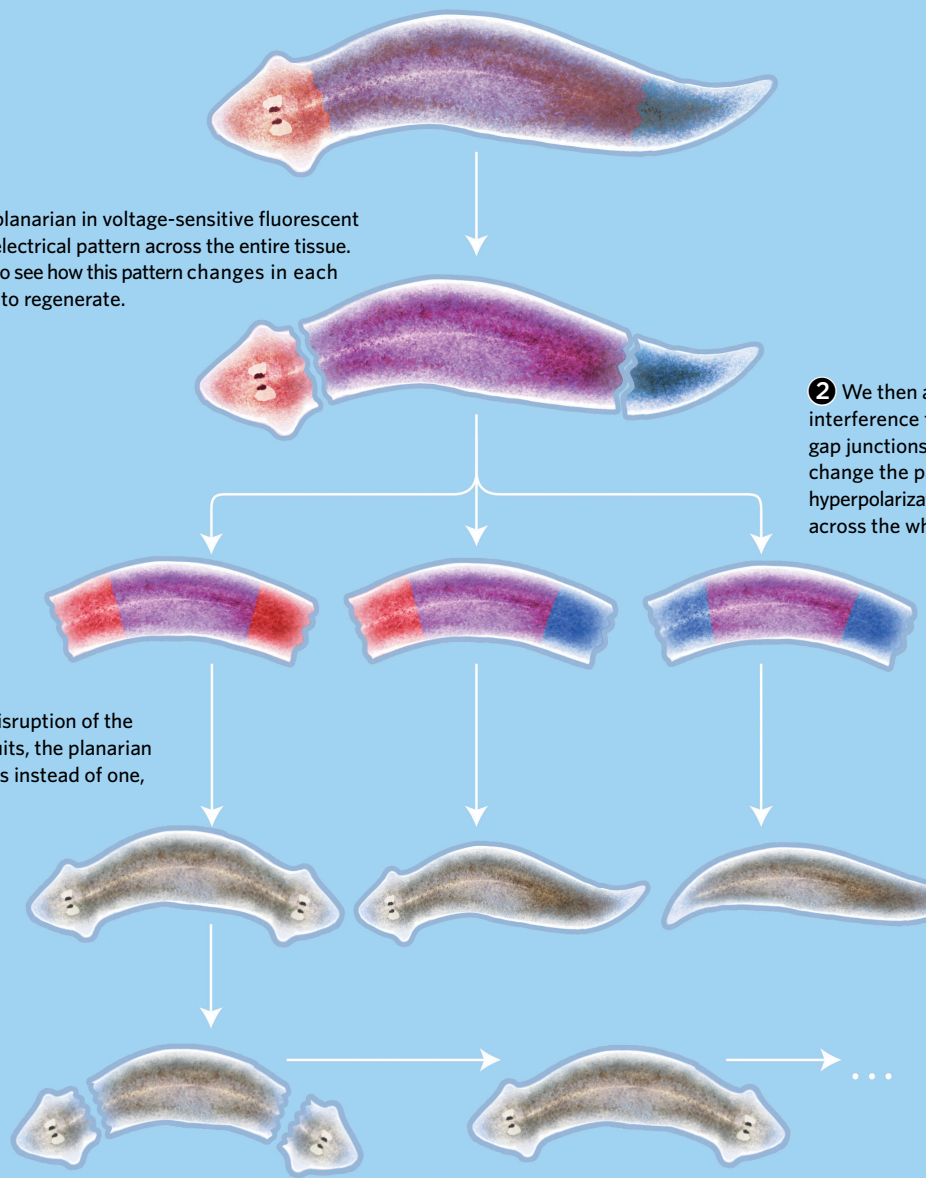
REWRITING THE PLANARIAN BODY PLAN

Recent work from our group and others has demonstrated that anatomical pattern memories can be rewritten by physiological stimuli and maintained indefinitely without genomic editing. For example, the bioelectric circuit that normally determines head number and location in regenerating planaria can be triggered by brief alterations of ion channel or gap junction activity to alter the animal's body plan. Due to the circuit's pattern memory, the animals remain in this altered state indefinitely without further stimulation, despite their wildtype genomes. In other words, the pattern to which the cells build after damage can be changed, leading to a target morphology distinct from the genetic default.



❶ First, we soaked a planarian in voltage-sensitive fluorescent dye to observe the bioelectrical pattern across the entire tissue. We then cut the animal to see how this pattern changes in each fragment as it begins to regenerate.

❷ We then applied drugs or used RNA interference to target ion channels or gap junctions in individual cells and thus change the pattern of depolarization/hyperpolarization and cellular connectivity across the whole fragment.

❸ As a result of the disruption of the body's bioelectric circuits, the planarian regrows with two heads instead of one, or none at all.

❹ When we re-cut the two-headed planarian in plain water, long after the initial drug has left the tissue, the new anatomy persists in subsequent rounds of regeneration.