# Comparing mathematical models of NSC Dynamics in Zebrafish against the Mouse

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Observations

## Adult mouse

- NSCs numbers decline with age in the DG and V-SVZ

## Adult zebrafish

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## Adult zebrafish

- NSCs in homologous neurogenic territories are maintained in numbers and proportions (homeostasis)

# Observations

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- Mathematical model of NSC dynamics

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Article | Open access | Published: 26 July 2025

**Unraveling regulatory feedback mechanisms in adult neurogenesis through mathematical modelling**

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**2922** Accesses | **2** Citations | **1** Altmetric | Metrics

## Adult zebrafish

- NSCs in homologous neurogenic territories are maintained in numbers and proportions (homeostasis)

Same?

Slightly different?

Completely different?

# Biological Context: NSCs anatomy and lineage progression in the fish brain

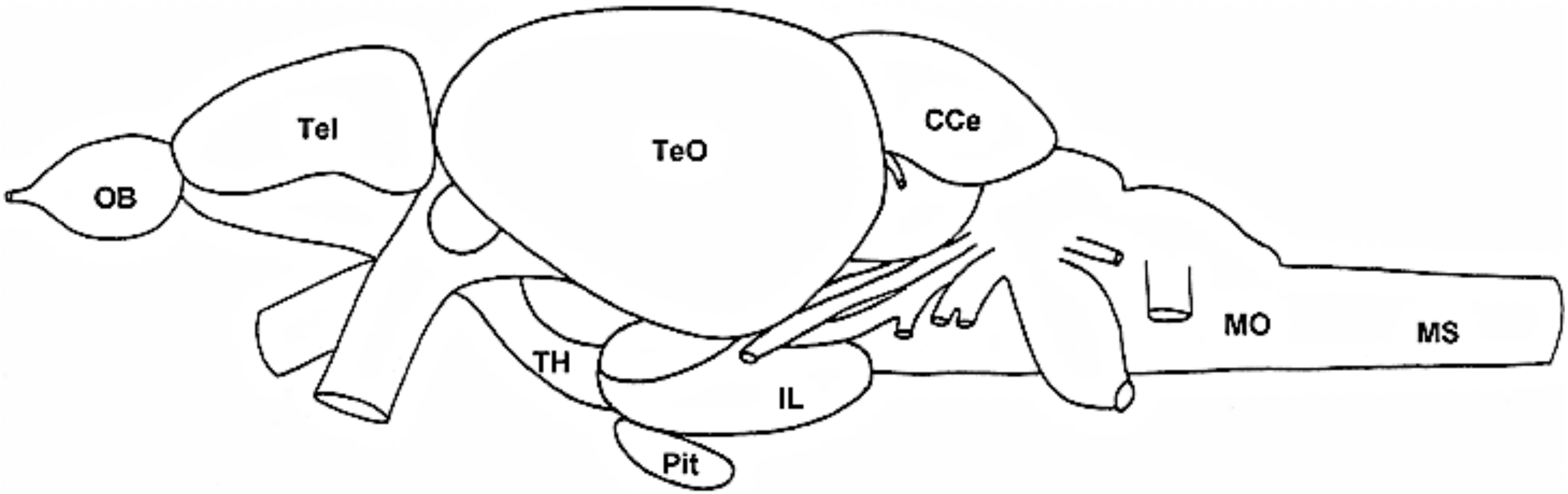


**Figure: Lateral view of the adult zebrafish brain (*credit to Daniel R. Dietrich*)**

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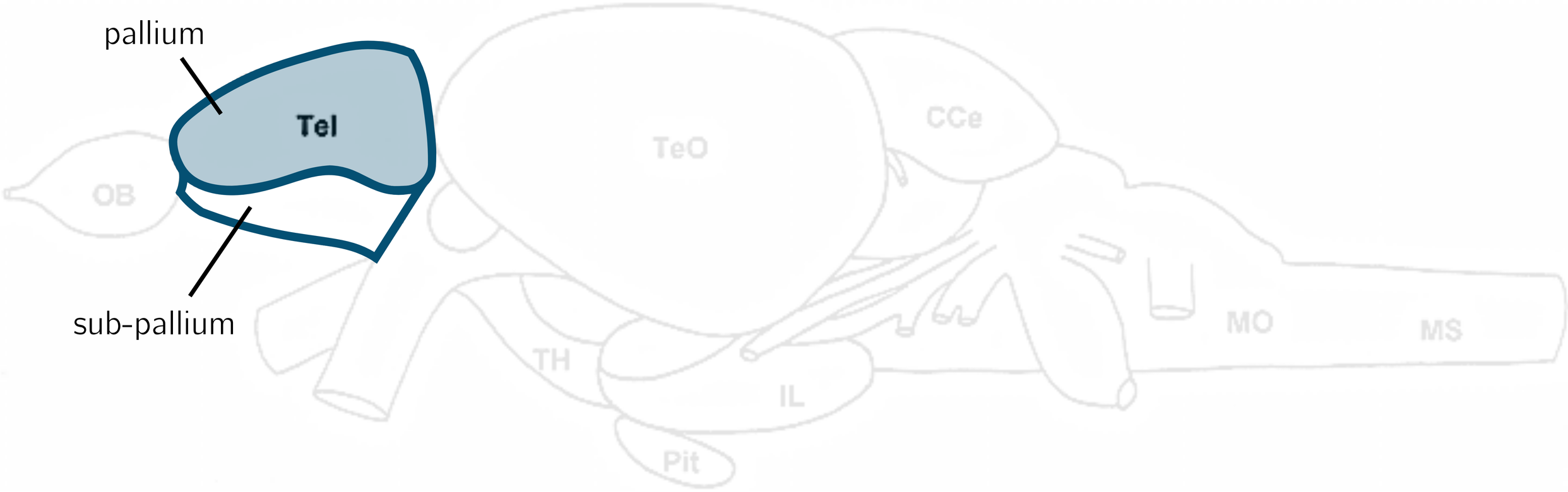


**Figure: Lateral view of the adult zebrafish brain (*credit to Daniel R. Dietrich*)**

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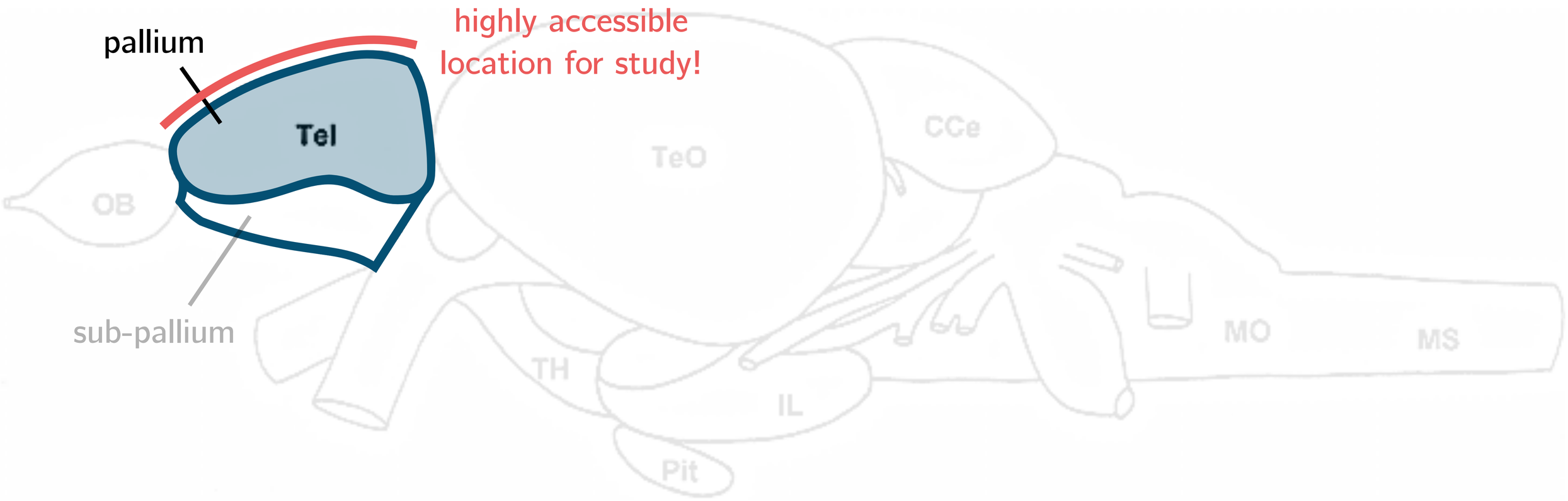


**Figure: Lateral view of the adult zebrafish brain (*credit to Daniel R. Dietrich*)**

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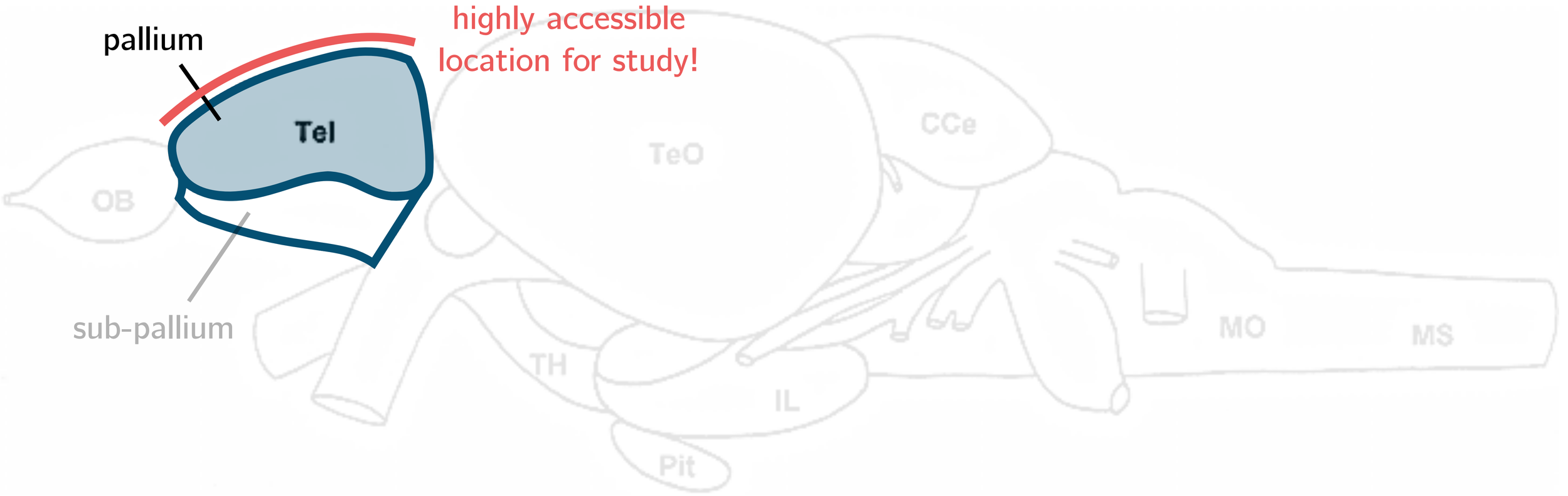



**Figure: Lateral view of the adult zebrafish brain (*credit to Daniel R. Dietrich*)**

Radial glia as NSCs:
GFAP/S100β/GS
Her4 (=Hes5)
Sox2

# Biological Context: NSCs anatomy and lineage progression in the fish brain

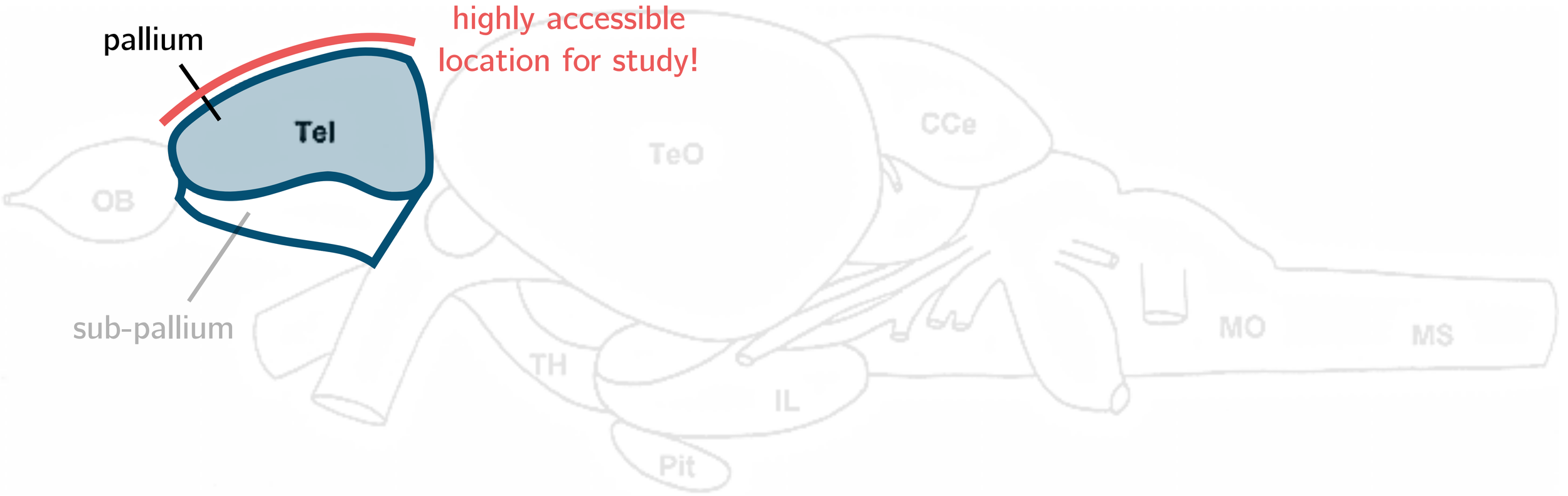



**Figure: Lateral view of the adult zebrafish brain (*credit to Daniel R. Dietrich*)**

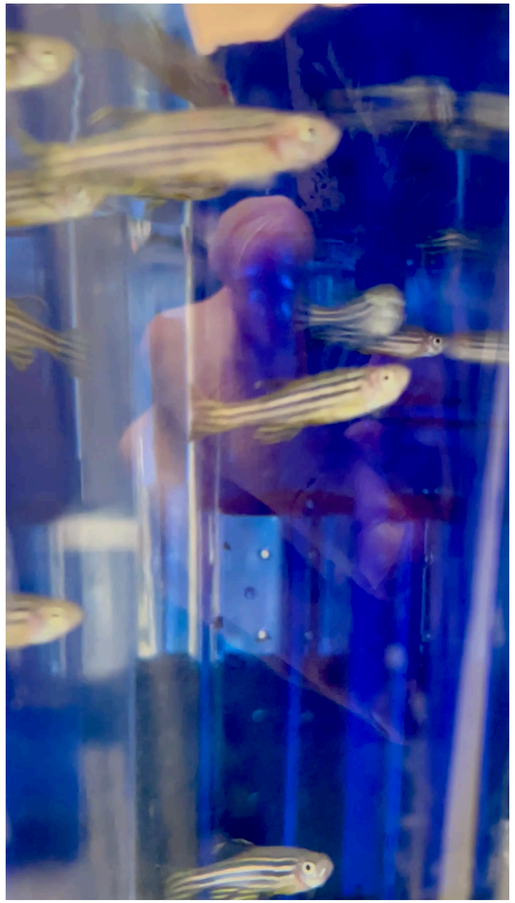
Radial glia as NSCs:
GFAP/S100β/GS
Her4 (=Hes5)
Sox2


$\cong$

SVZ/SEZ of the lateral ventricle
and
DG of the hippocampus

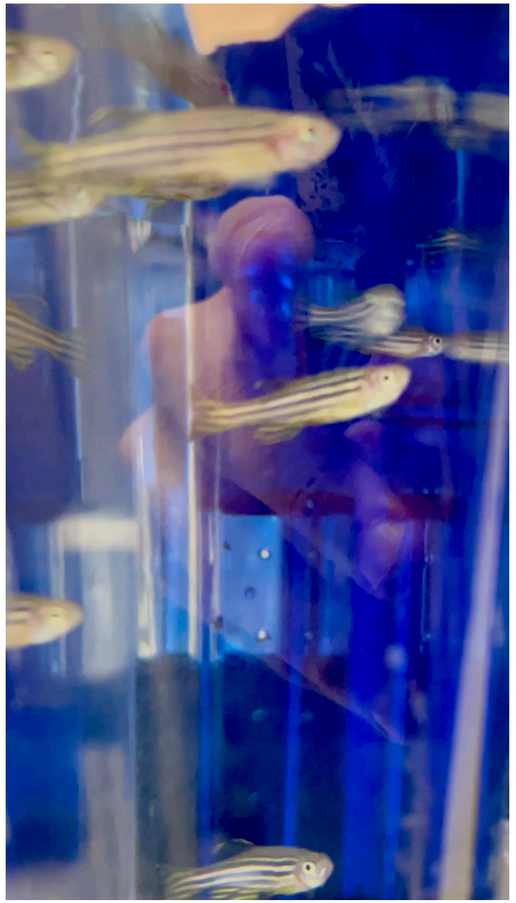
# Biological Context: NSCs anatomy and lineage progression in the fish brain

**Wild Type**



# Biological Context: NSCs anatomy and lineage progression in the fish brain

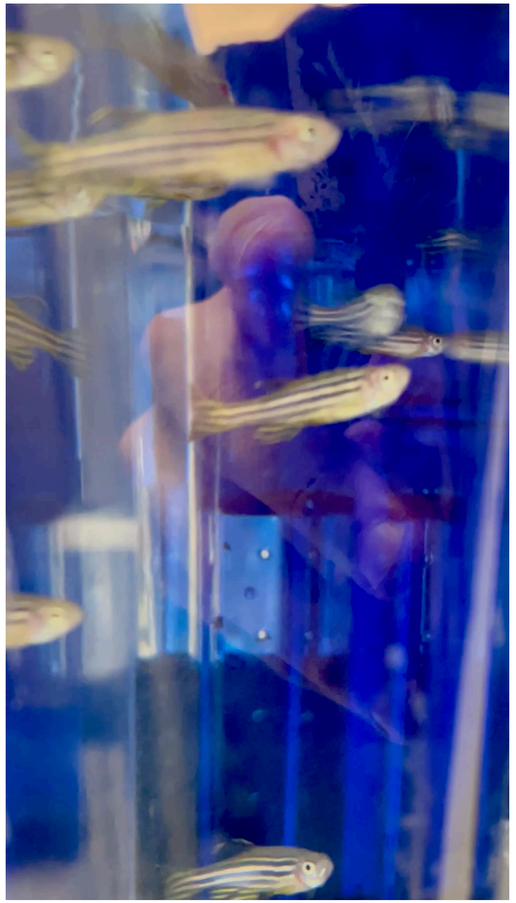
**Wild Type**



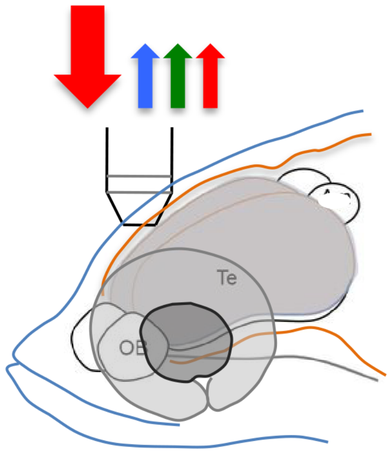
**Mutant**

# Biological Context: NSCs anatomy and lineage progression in the fish brain

**Wild Type**

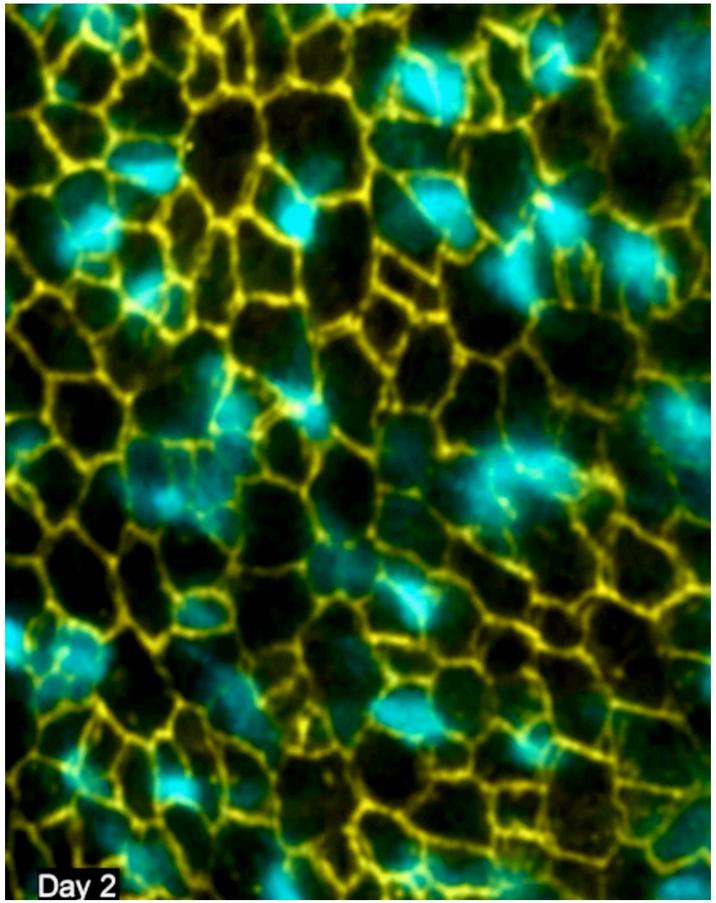


**Mutant**




(*credit to Laure Bally-Cuif*)

**Pallial NSC population**

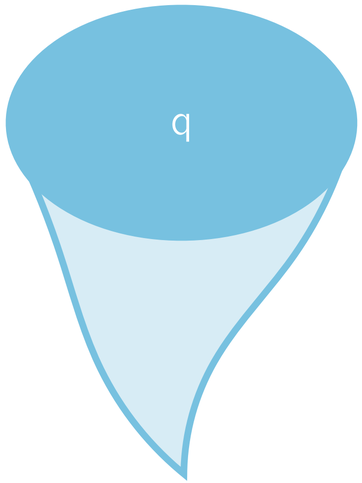



source: https://doi.org/10.1126/sciadv.adg7519

# Biological Context: NSCs anatomy and lineage progression in the fish brain

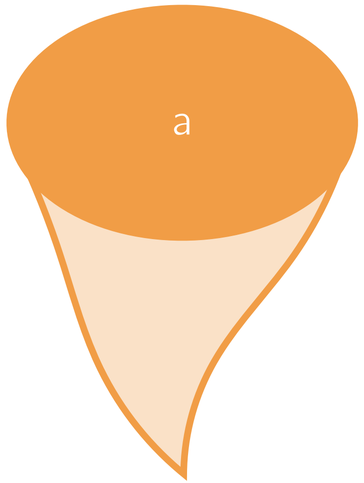
**dIA-neg cells (reservoir)**

- slow dynamics
- population-amplifying role




Quiescent Reservoir NSC

(Gfap+, Sox2+, PCNA-, dIA-)

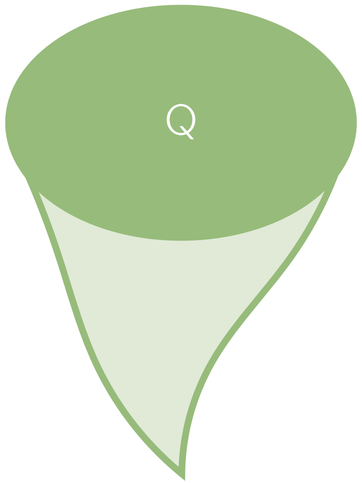



Active Reservoir NSC

(Gfap+, Sox2+, PCNA+, dIA-)

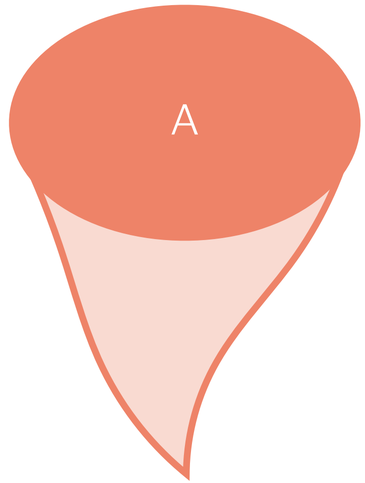
**dIA-pos cells (operational)**

- fast dynamics
- neuron-producing role



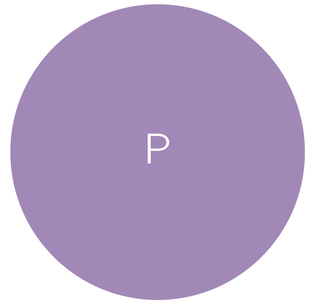

Quiescent Operational NSC

(Gfap+, Sox2+, PCNA-, dIA+)




Active Operational NSC

(Gfap+, Sox2+, PCNA+, dIA+)



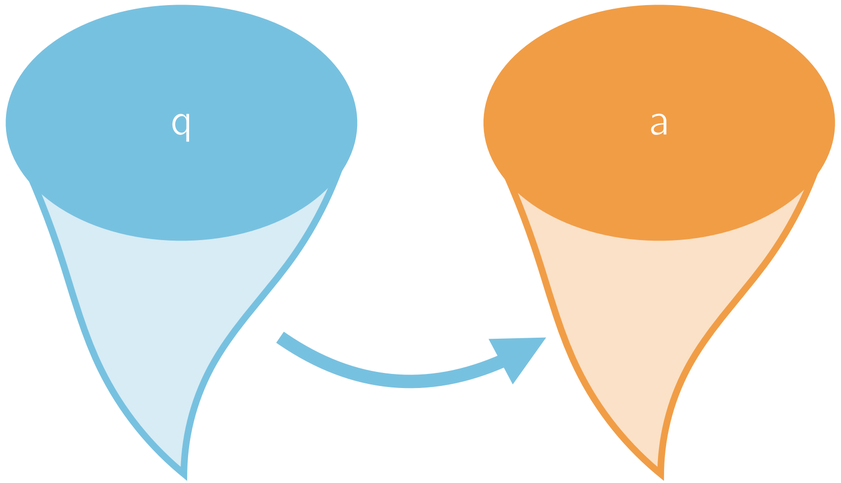

Neural Progenitor

(Gfap-, Sox2+, PCNA+, dIA+)

# Biological Context: NSCs anatomy and lineage progression in the fish brain

**dIA-neg cells (reservoir)**

- slow dynamics
- population-amplifying role




Quiescent Reservoir NSC

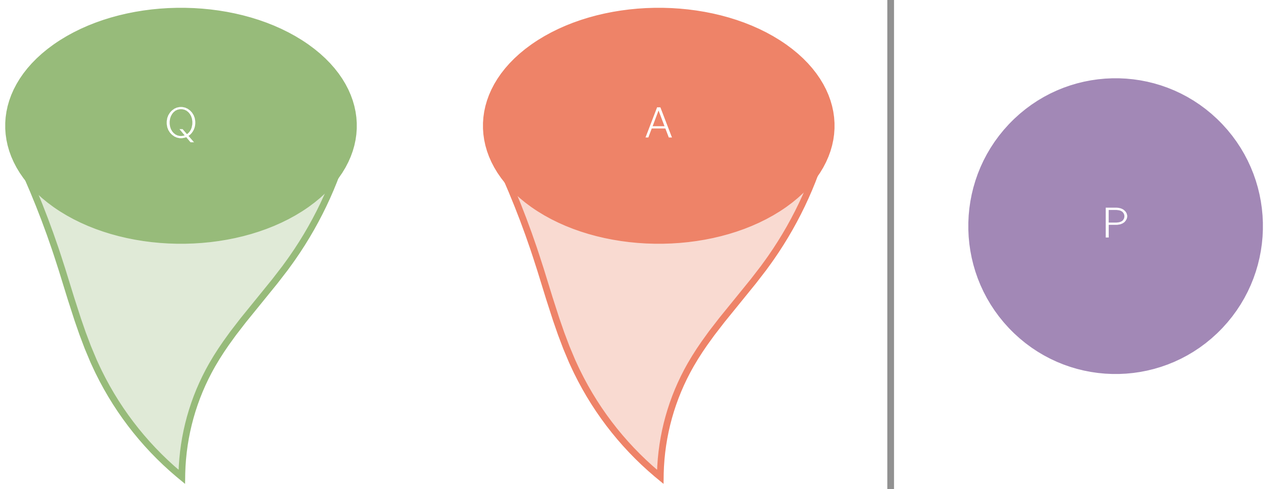
(Gfap+, Sox2+, PCNA-, dIA-)

Active Reservoir NSC

(Gfap+, Sox2+, PCNA+, dIA-)

**dIA-pos cells (operational)**

- fast dynamics
- neuron-producing role




Quiescent Operational NSC

(Gfap+, Sox2+, PCNA-, dIA+)

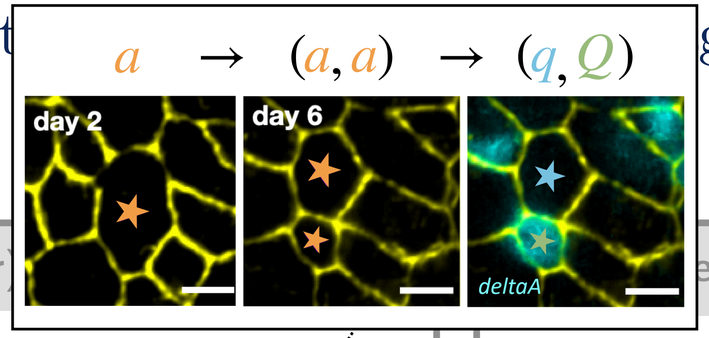
Active Operational NSC

(Gfap+, Sox2+, PCNA+, dIA+)

Neural Progenitor

(Gfap-, Sox2+, PCNA+, dIA+)

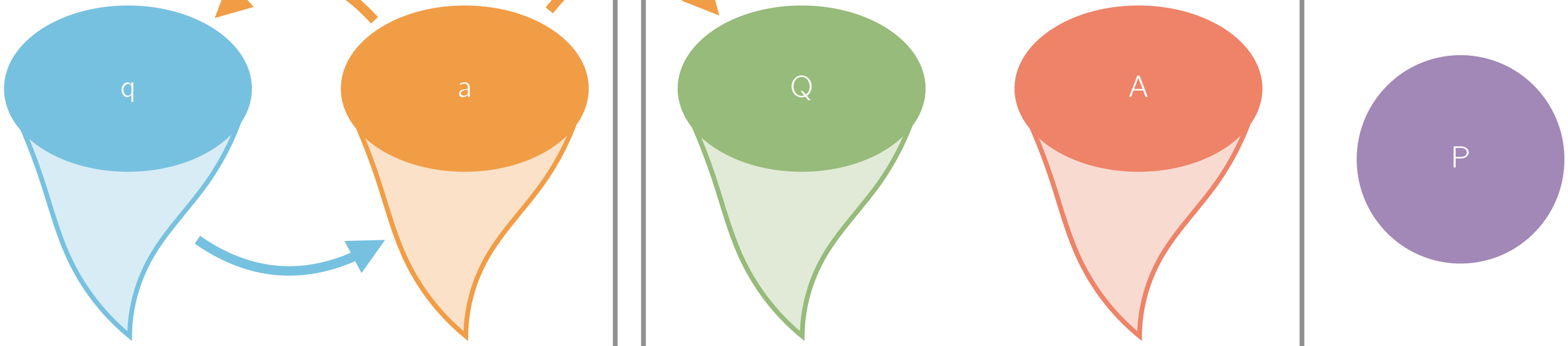
# Biological Context: Cell lineage progression in the fish brain




dIA-neg cells (reservoir) | dIA+ cells (operational)

- slow dynamics
- population-amplifying role

- fast dynamics
- neuron-producing role




**Quiescent Reservoir NSC**
(Gfap+, Sox2+, PCNA-, dIA-)

**Active Reservoir NSC**
(Gfap+, Sox2+, PCNA+, dIA-)

**Quiescent Operational NSC**
(Gfap+, Sox2+, PCNA-, dIA+)

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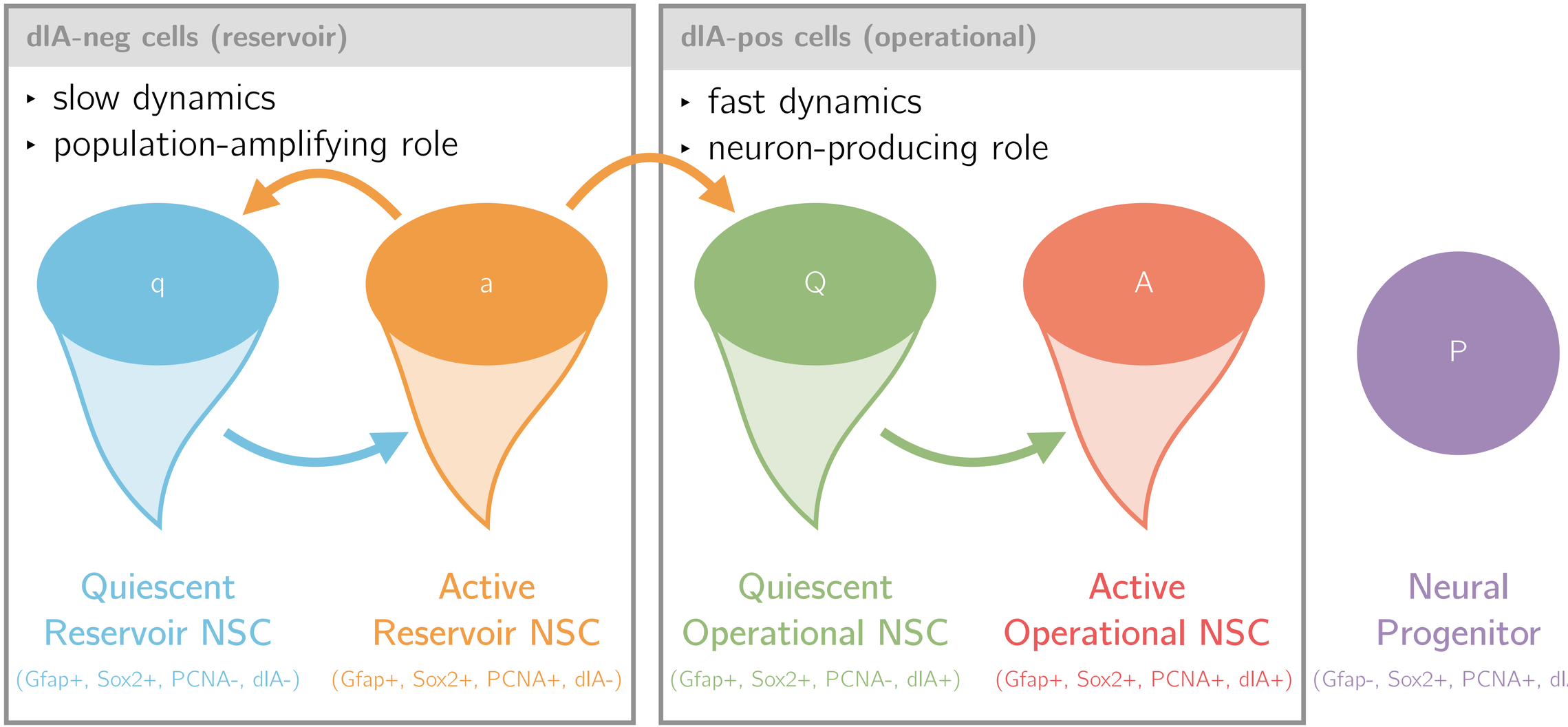
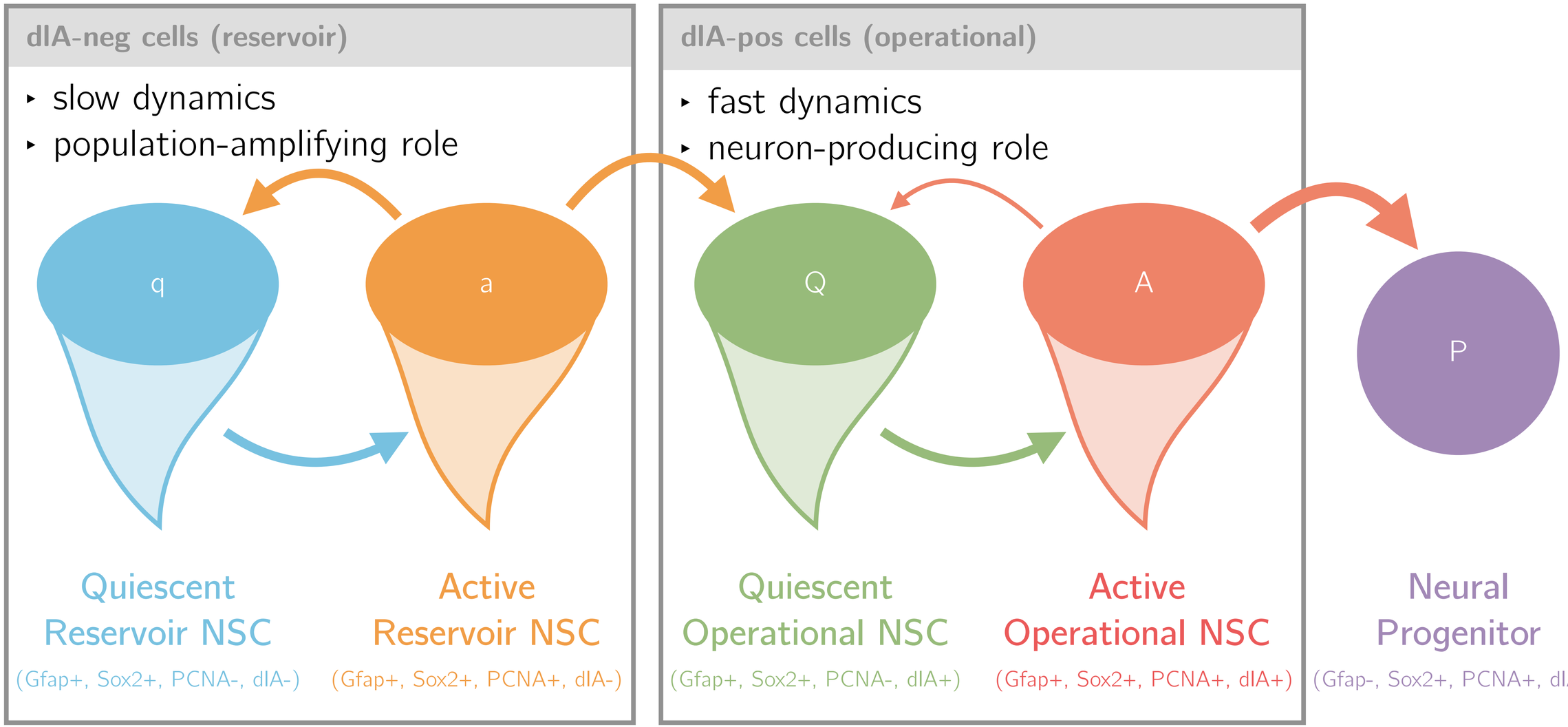
**Neural Progenitor**
(Gfap-, Sox2+, PCNA+, dIA+)

# Biological Context: NSCs anatomy and lineage progression in the fish brain



# Biological Context: NSCs anatomy and lineage progression in the fish brain



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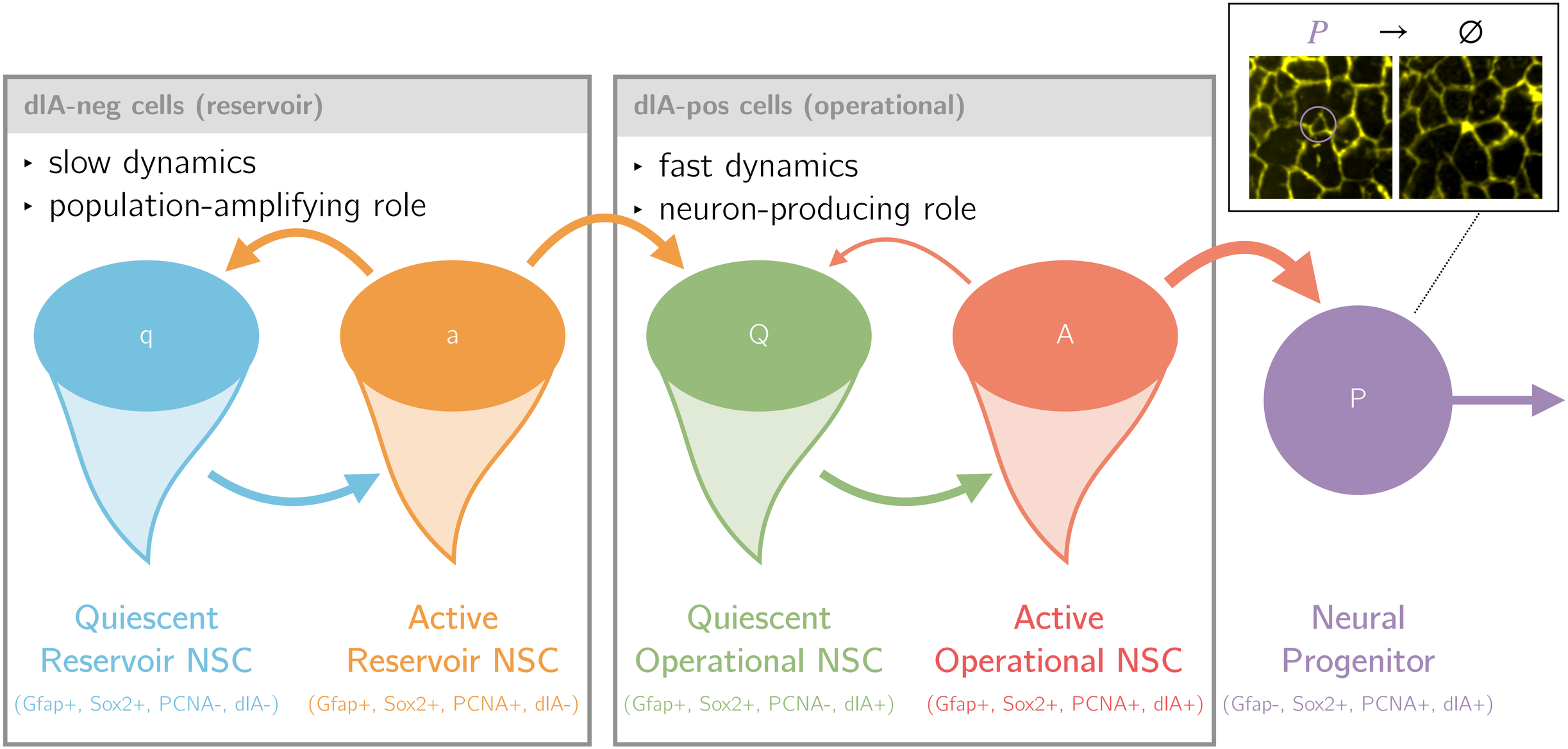


# Model Visualization: Compartmental evolution

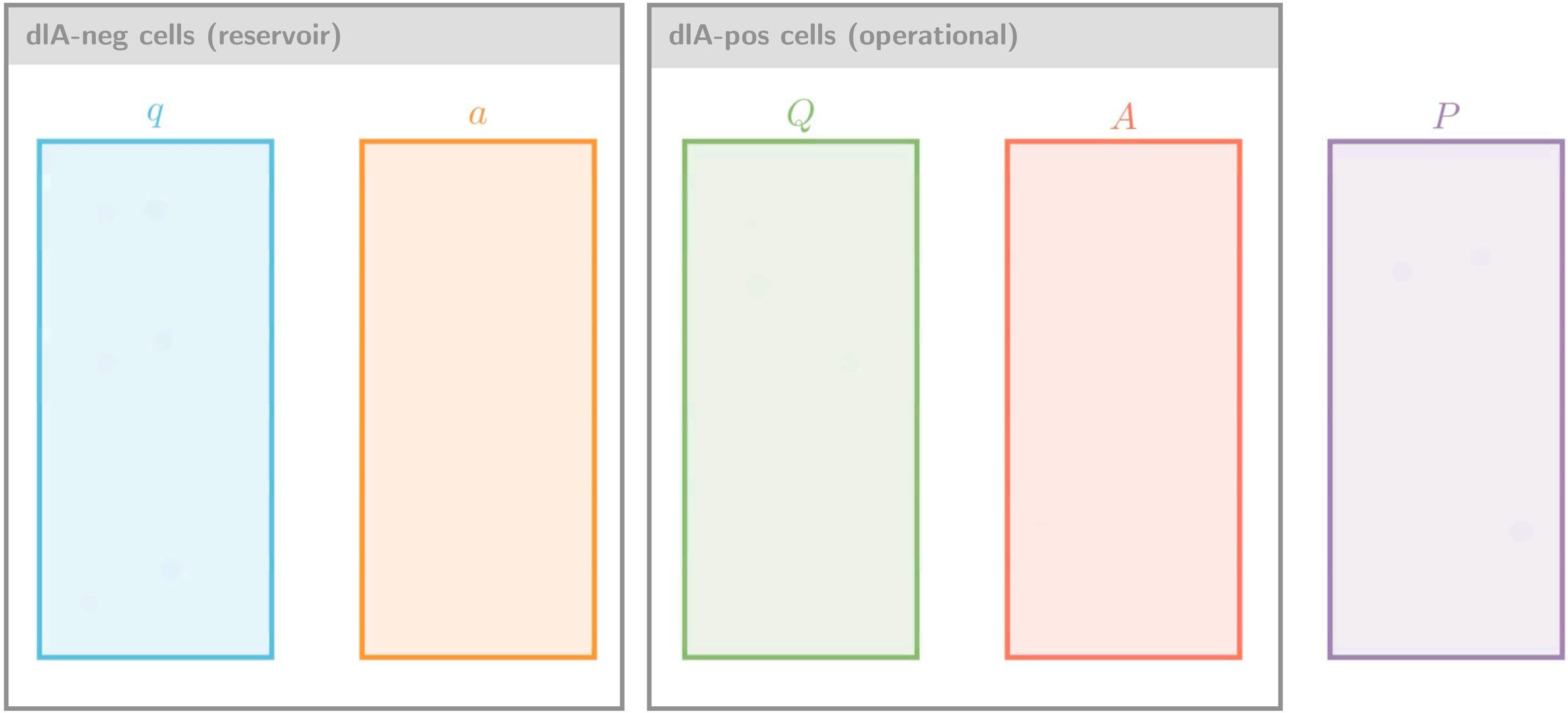
Step 1: Define state variables (who's who)

**dIA-neg cells (reservoir)**

**dIA-pos cells (operational)**

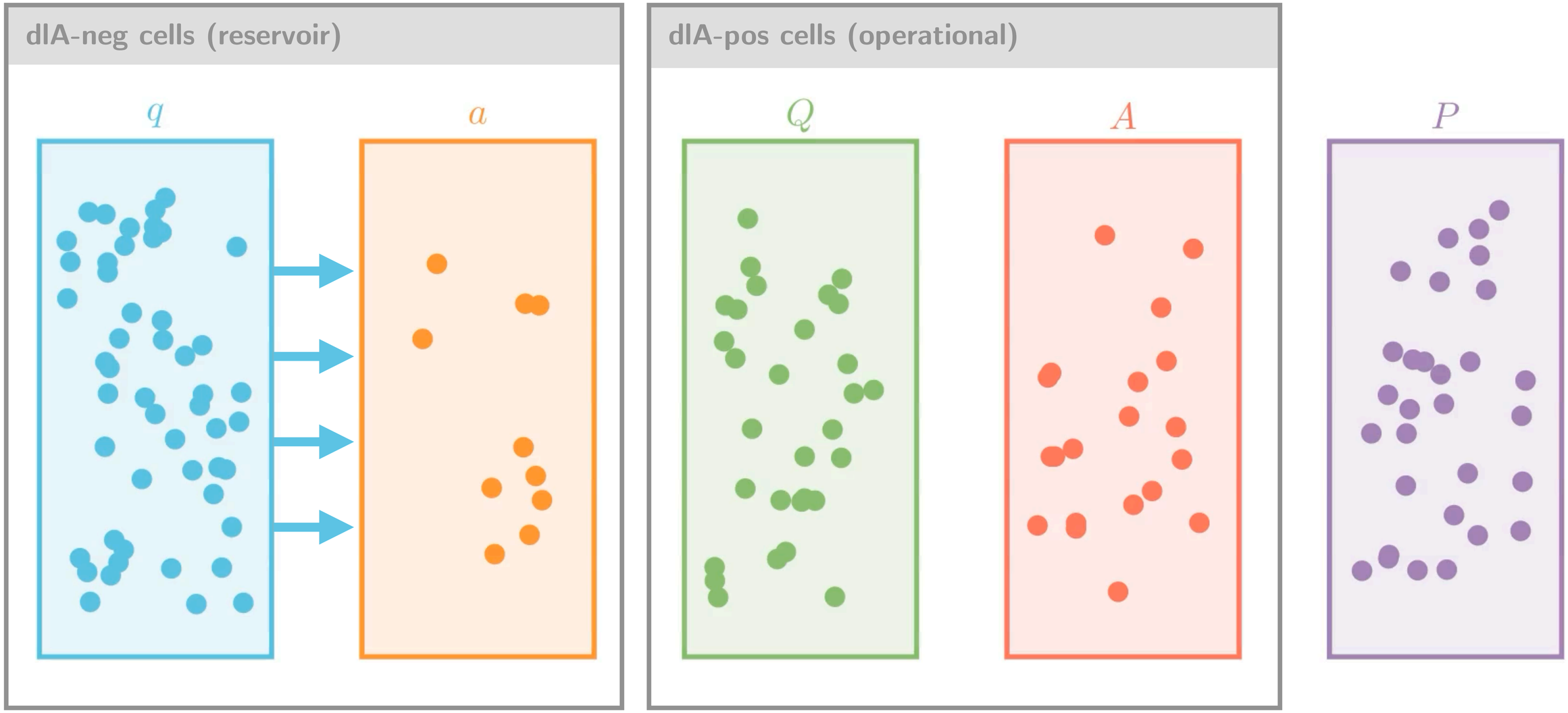
# Model Visualization: Compartmental evolution

Step 2: Populate each compartment (initial condition)



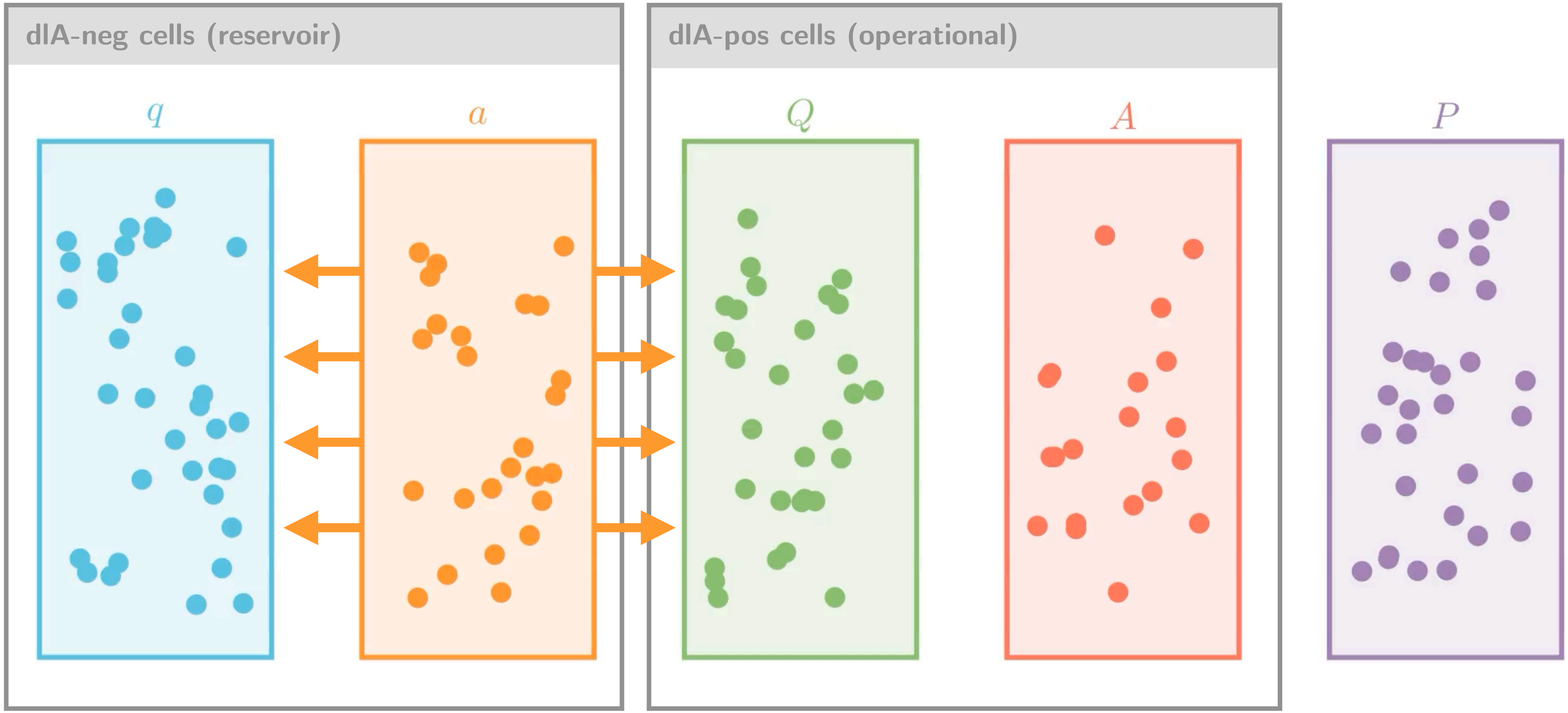
# Model Visualization: Compartmental evolution

Step 3.a: reservoir qNSC activate ($q'(t) = -r_0 q(t)$ and $a'(t) = +r_0 q(t)$)



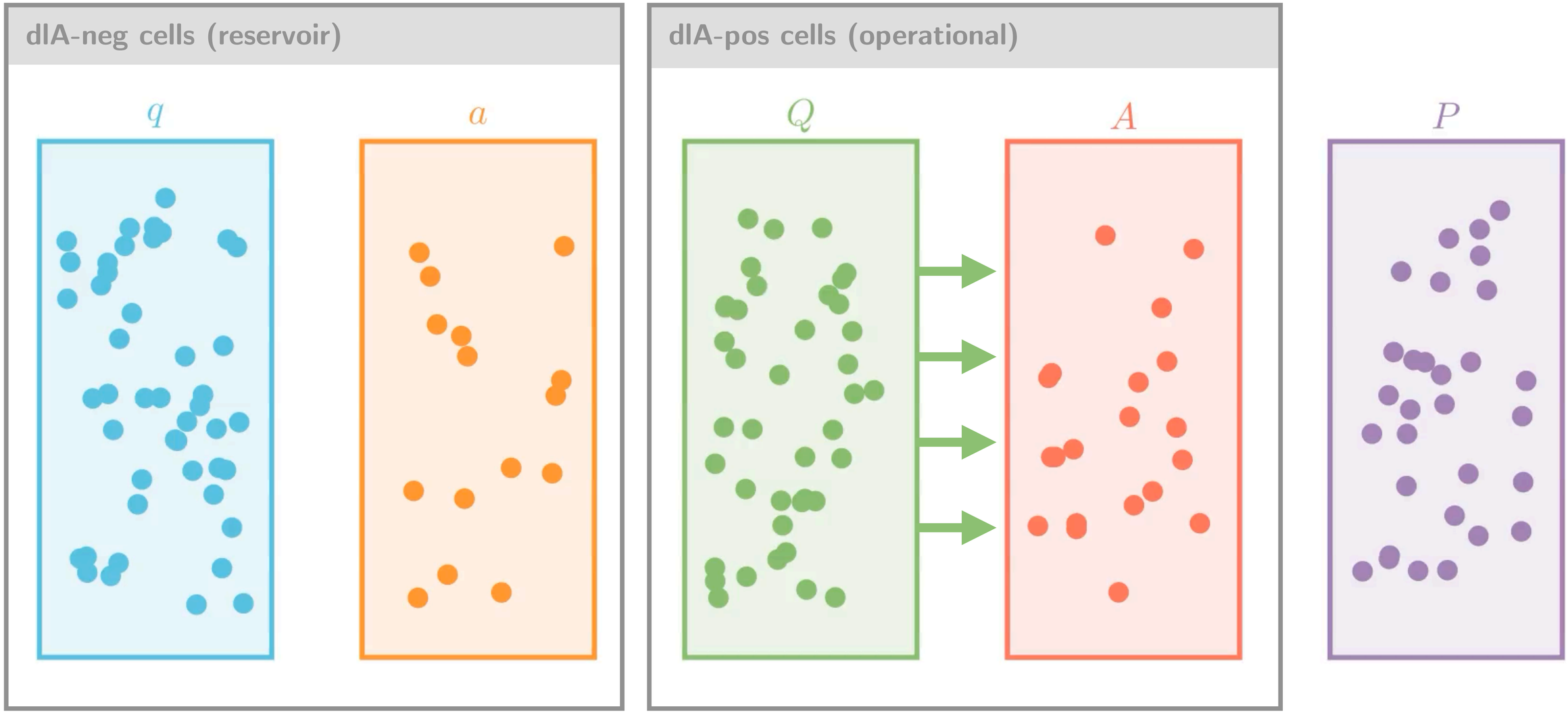
# Model Visualization: Compartmental evolution

Step 3.b: reservoir aNSC divide asymmetrically ($a'(t) = -pa(t)$, $q'(t) = +pa(t)$, and $Q'(t) = +pa(t)$)



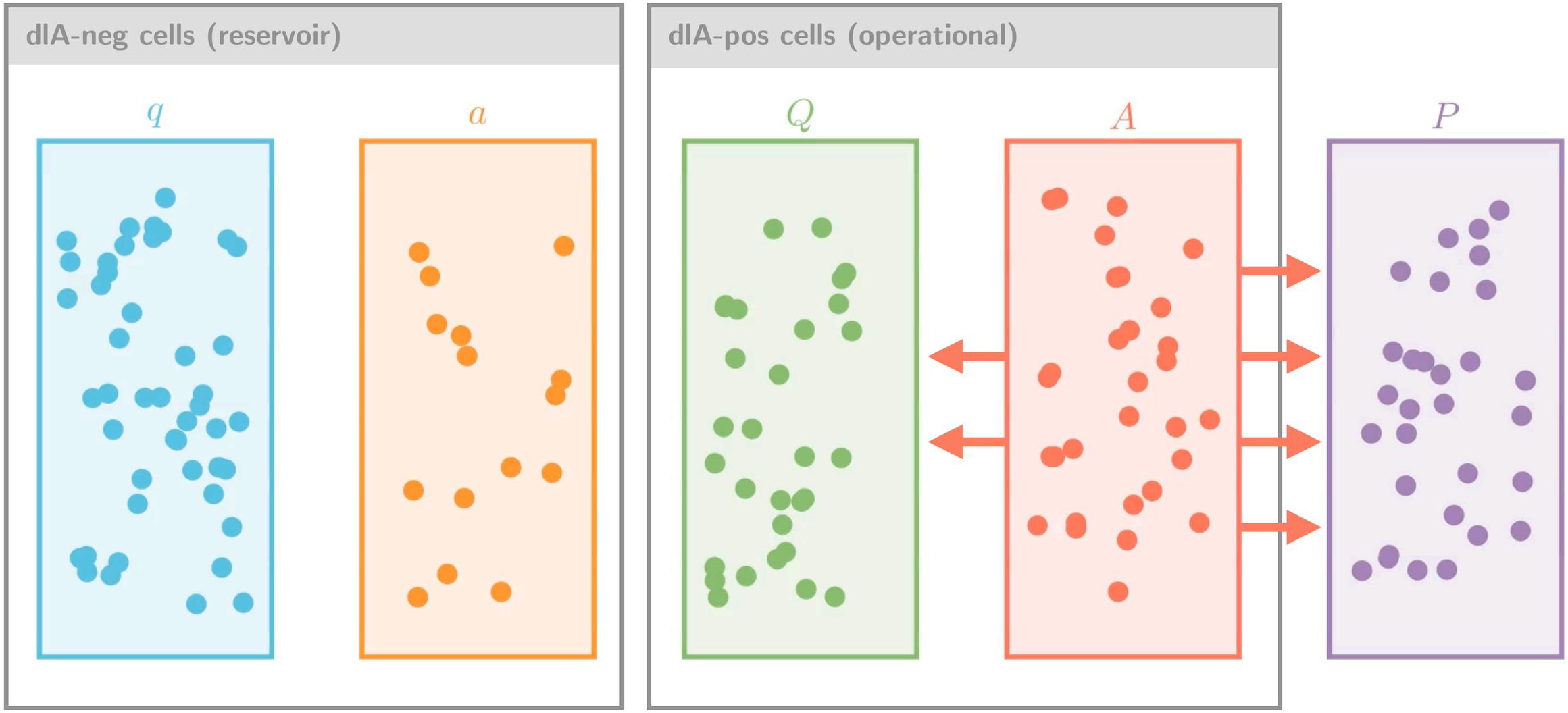
# Model Visualization: Compartmental evolution

Step 3.c: operational qNSC activate ($Q'(t) = -r_1 Q(t)$, and $A(t) = +r_1 Q(t)$)



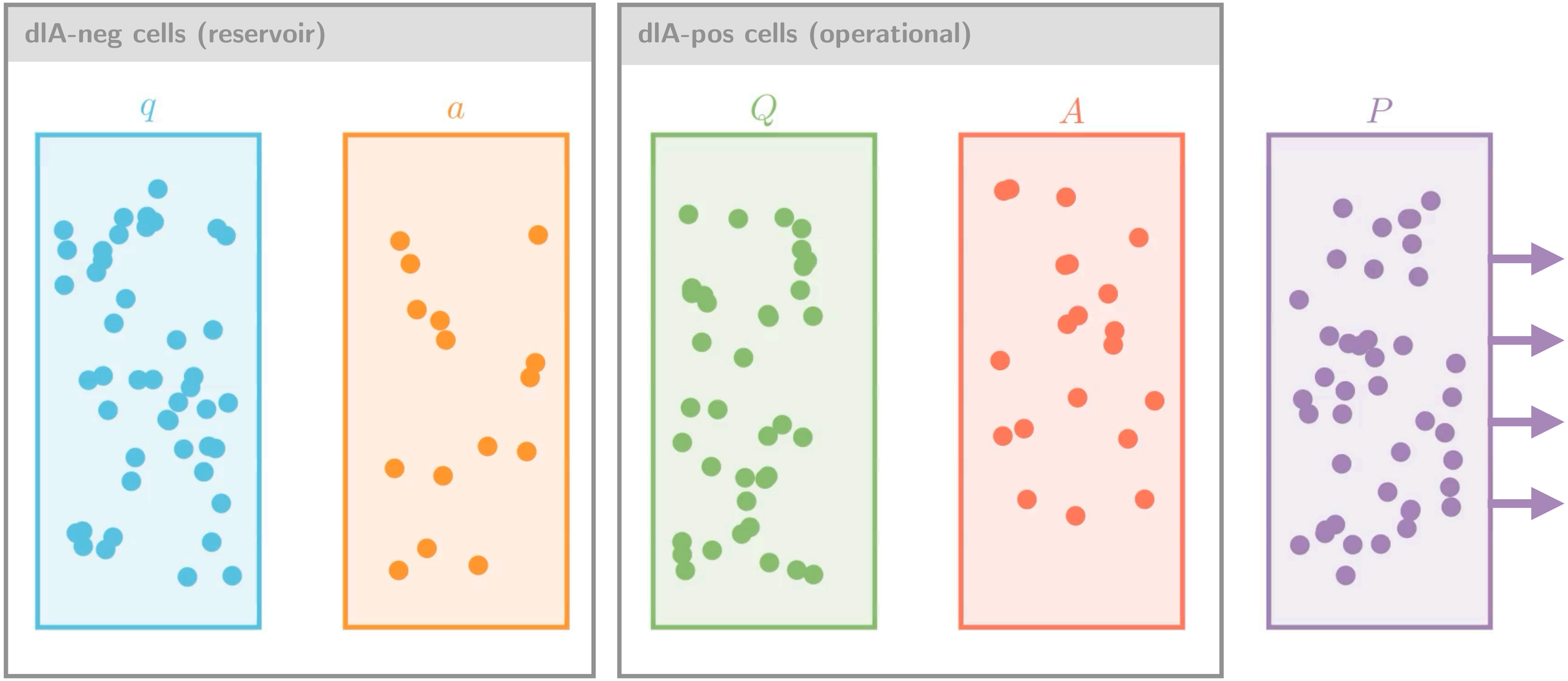
# Model Visualization: Compartmental evolution

Step 3.d: operational aNSC divide ($A'(t) = -pA(t)$, $Q'(t) = +2b_0pA(t)$, and $P'(t) = +2(1-b_0)pA(t)$)

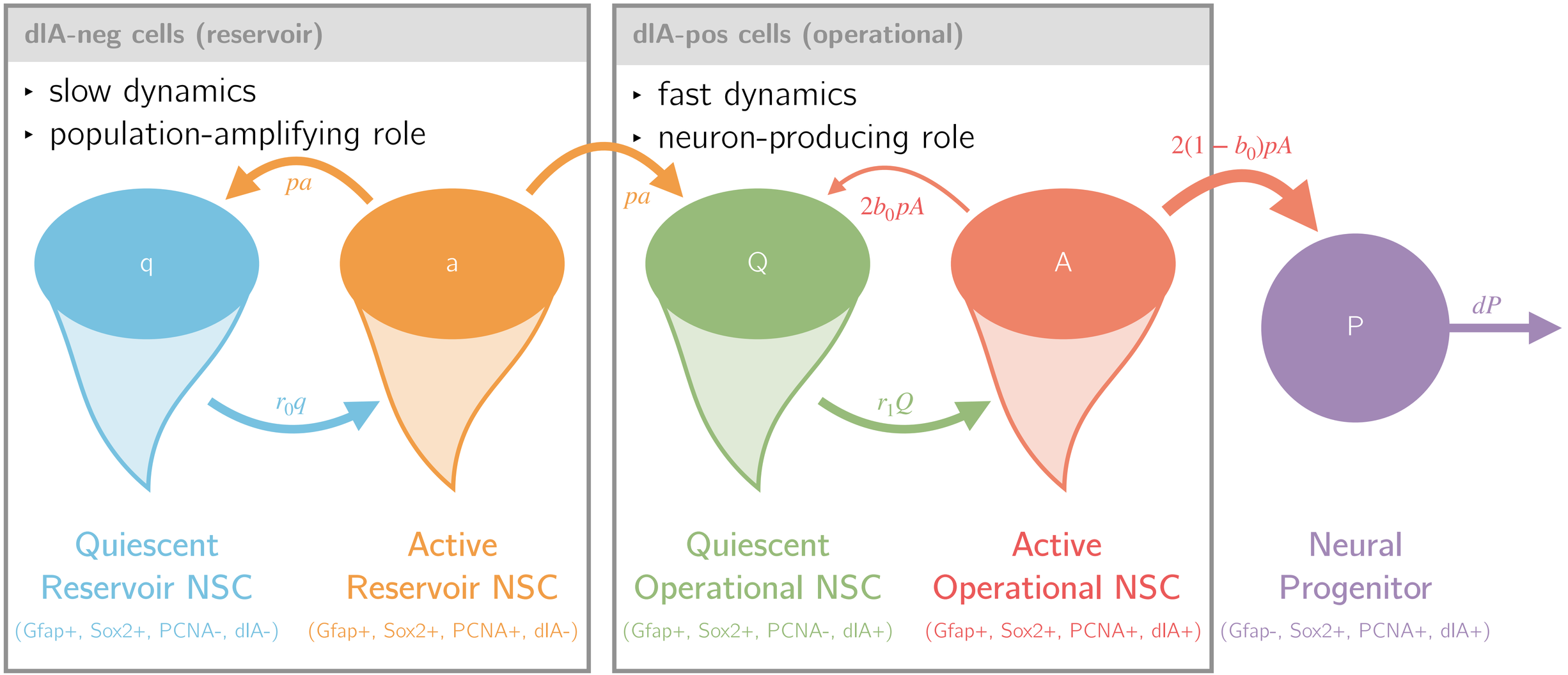


# Model Visualization: Compartmental evolution

Step 3.e: neural Progenitors delaminate ($P'(t) = -dP(t)$)



# Model Equations (Summary)



# Model Equations



**dIA-neg cells (reservoir)**

$$q'(t) = -r_0 q(t) + p a(t),$$

$$a'(t) = r_0 q(t) - p a(t),$$

**dIA-pos cells (operational)**



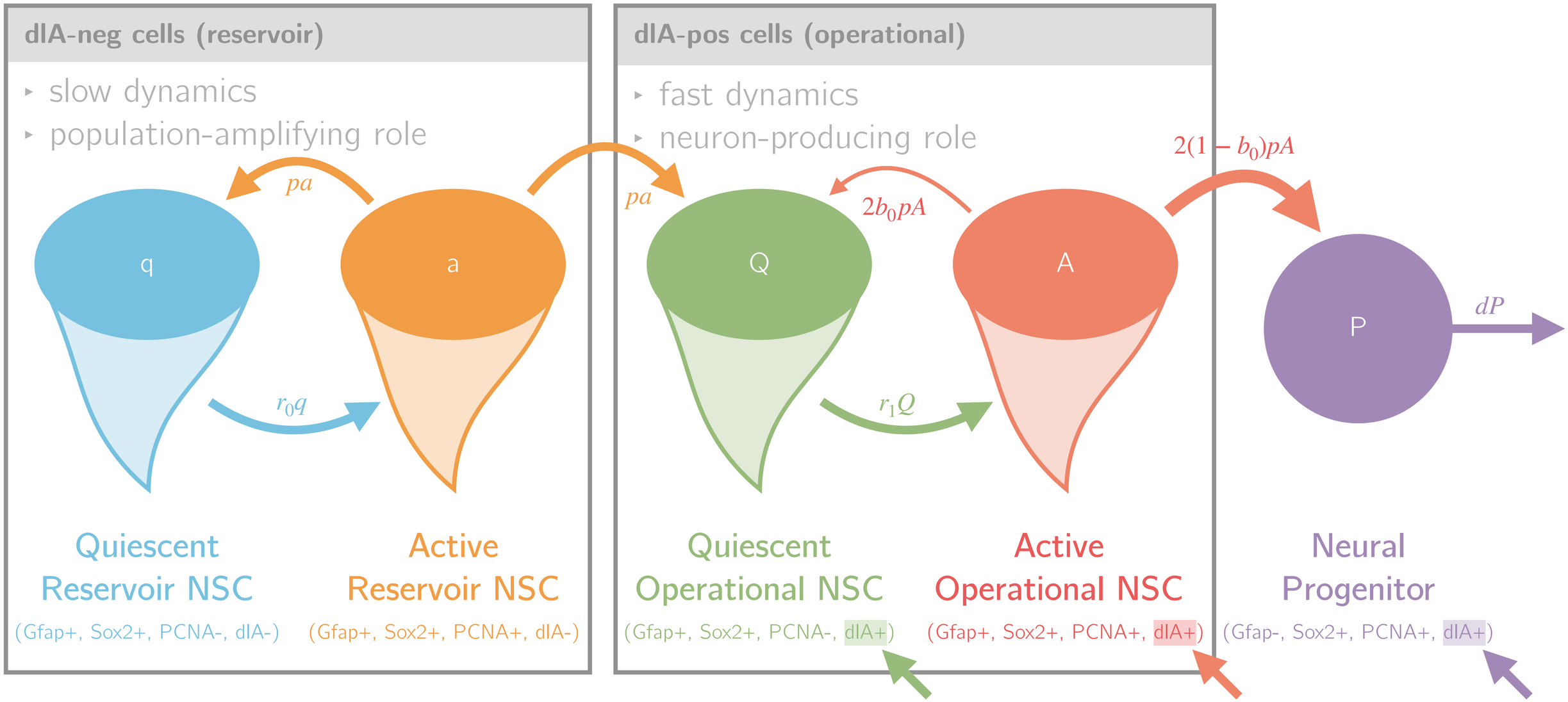
$$Q'(t) = -r_1 Q(t) + 2 b_0 p A(t) + p a(t),$$

$$A'(t) = r_1 Q(t) - p A(t),$$

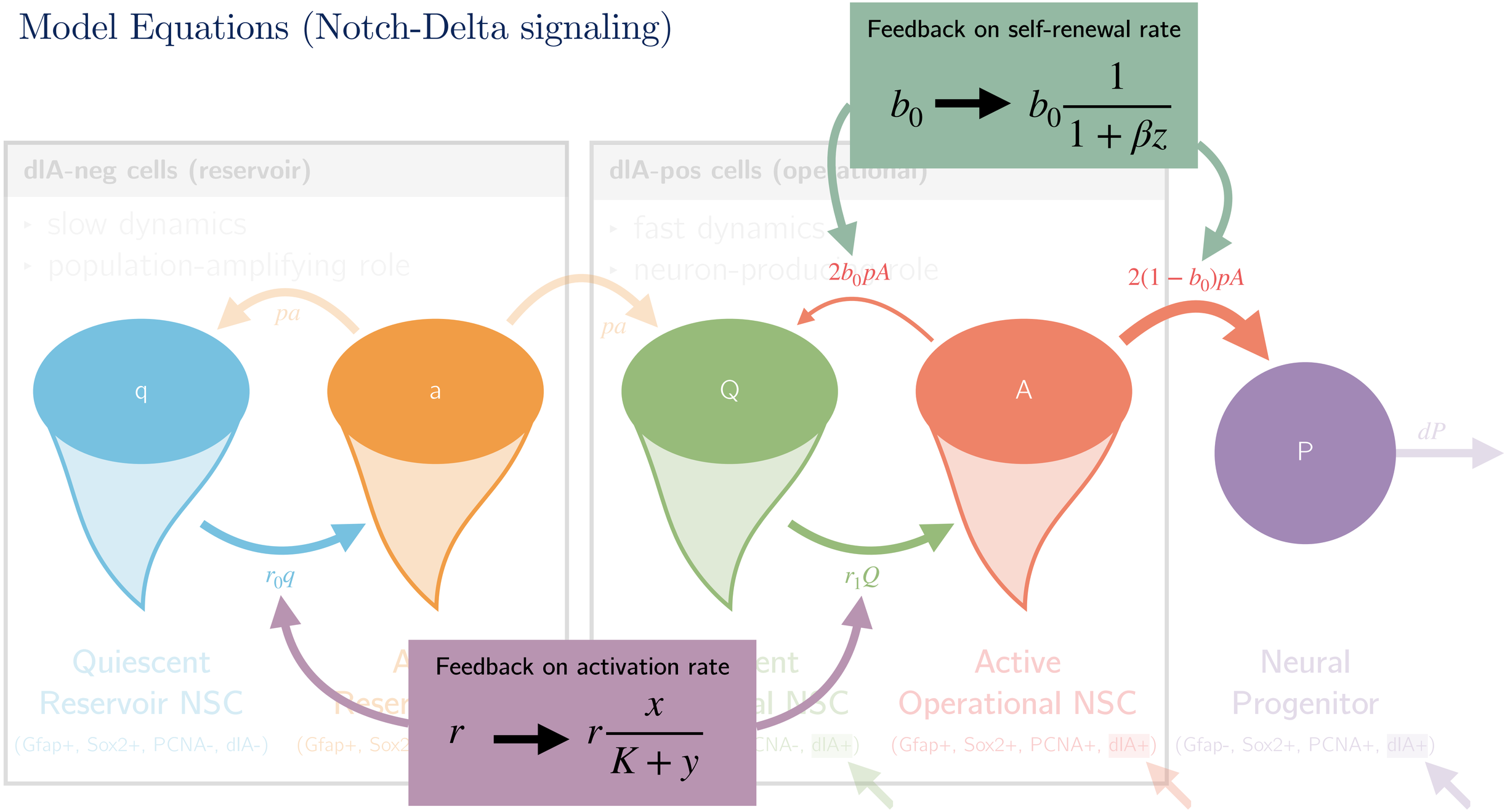

$$P'(t) = 2(1 - b_0) p A(t) - d P(t)$$

# Modeling Notch-delta Signaling

# Model Equations (Notch-Delta signaling)



# Model Equations (Notch-Delta signaling)





**dIA-neg cells (reservoir)**

$$q'(t) = -r_0 \frac{x(t)}{K + y(t)} q(t) + pa(t),$$

$$a'(t) = r_0 \frac{x(t)}{K + y(t)} q(t) - pa(t),$$



**dIA-pos cells (operational)**

$$Q'(t) = -r_1 \frac{x(t)}{K + y(t)} Q(t) + 2b_0 \frac{1}{1 + \beta z(t)} pA(t) + pa(t),$$

$$A'(t) = r_1 \frac{x(t)}{K + y(t)} Q(t) - pA(t),$$


$$P'(t) = 2 \left( 1 - b_0 \frac{1}{1 + \beta z(t)} \right) pA(t) - dP(t)$$






dIA-neg cells (reservoir)

$$q'(t) = -r_0 \frac{x(t)}{K + y(t)} q(t) + pa(t),$$

$$a'(t) = r_0 \frac{x(t)}{K + y(t)} q(t) - pa(t),$$

dIA-pos cells (operational)

$$Q'(t) = -r_1 \frac{x(t)}{K + y(t)} Q(t) + 2b_0 \frac{1}{1 + \beta z(t)} pA(t) + pa(t),$$

$$A'(t) = r_1 \frac{x(t)}{K + y(t)} Q(t) - pA(t),$$

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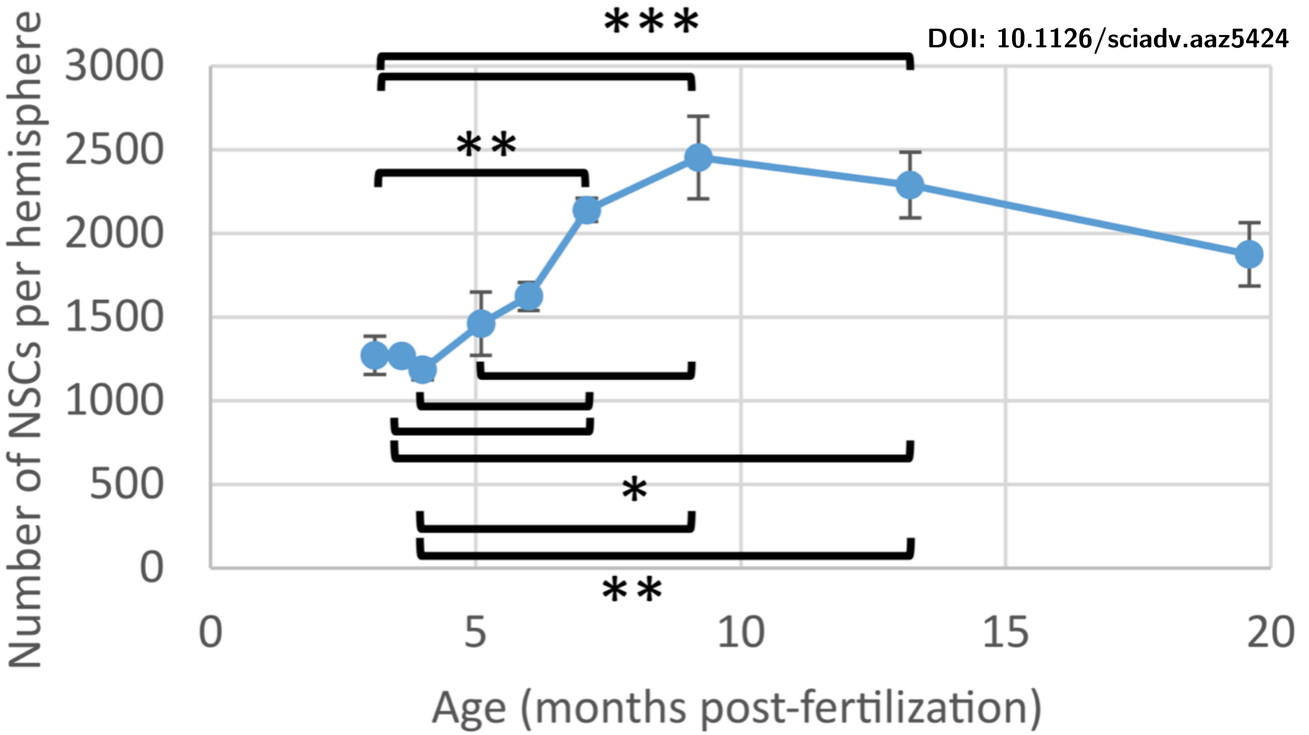
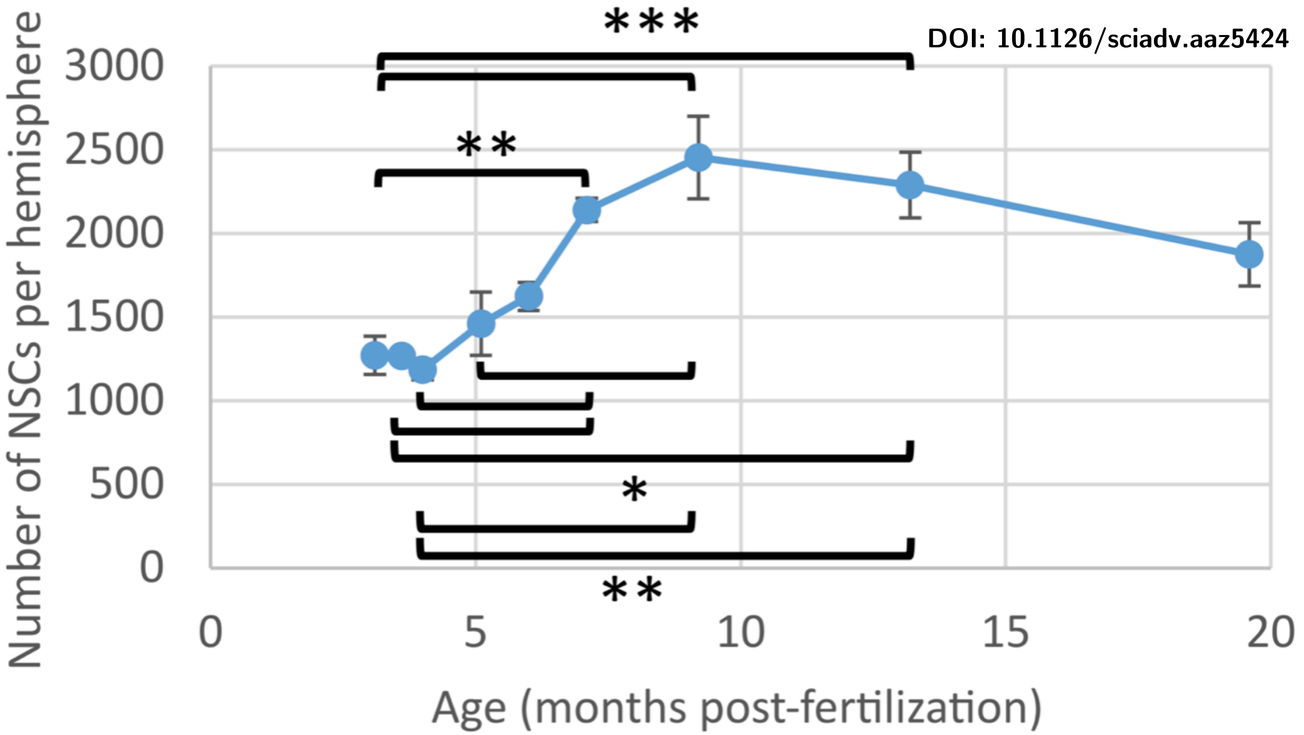
**Mouse System**

# Calibration: Investigating the data




a. Average number of cells per hemisphere (n=7 brains), reported by Sox2 expression (NSCs + NPs) over 500 days

## Calibration: Investigating the data

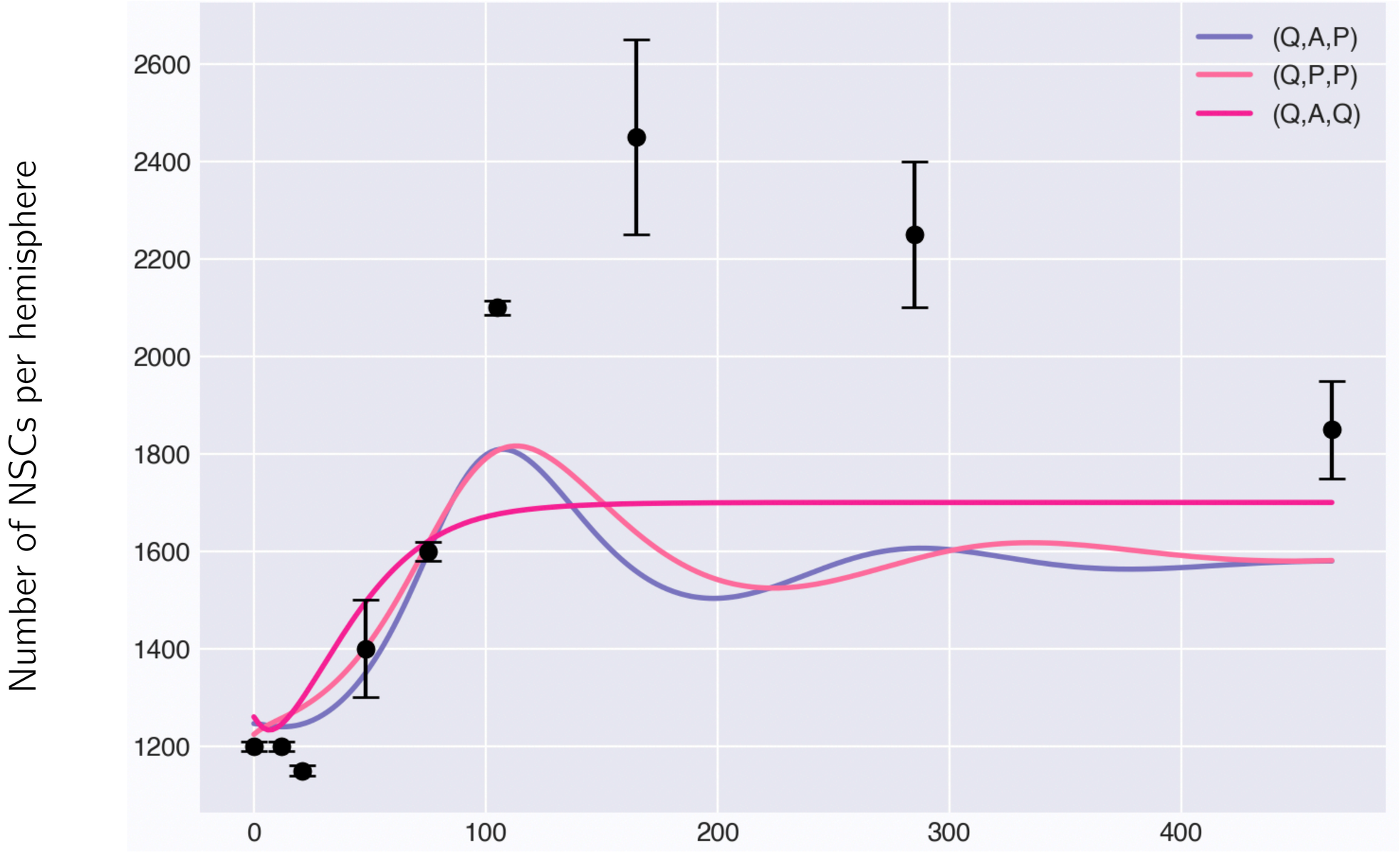



a. Average number of cells per hemisphere (n=7 brains), reported by Sox2 expression (NSCs + NPs) over 500 days

Provides a measure of

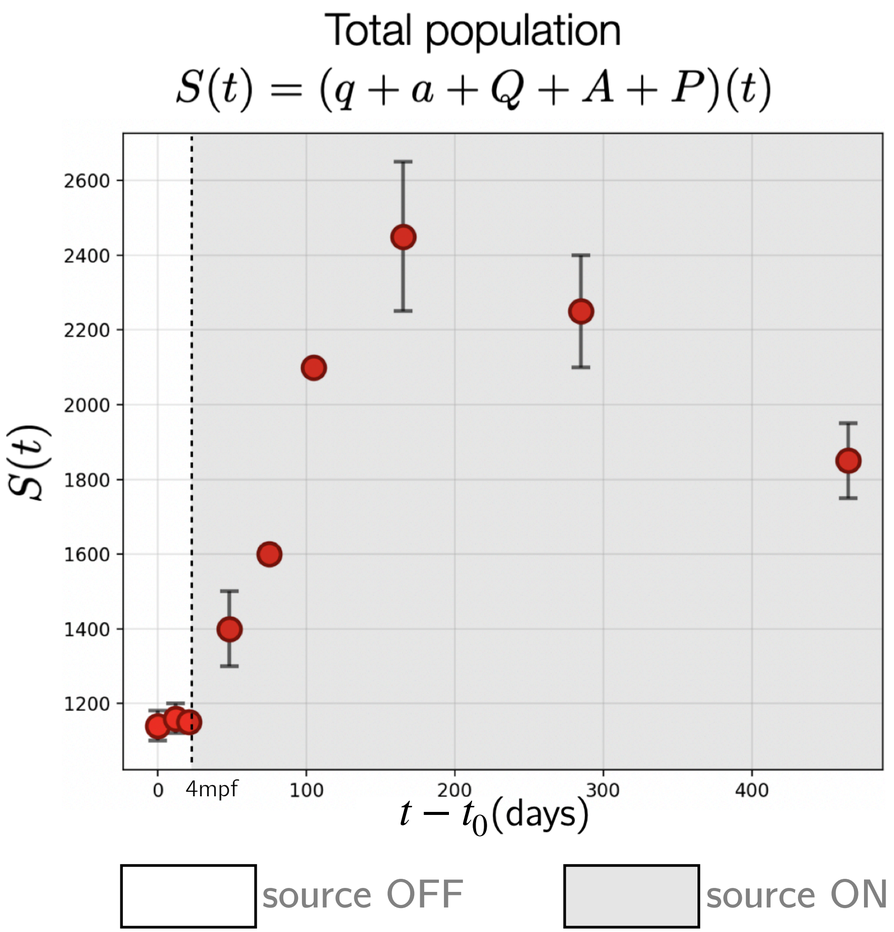
$$S(t) := q(t) + a(t) + Q(t) + A(t) + P(t)$$

# Comparison of multiple plausible scenarios for Notch-DeltaA signaling



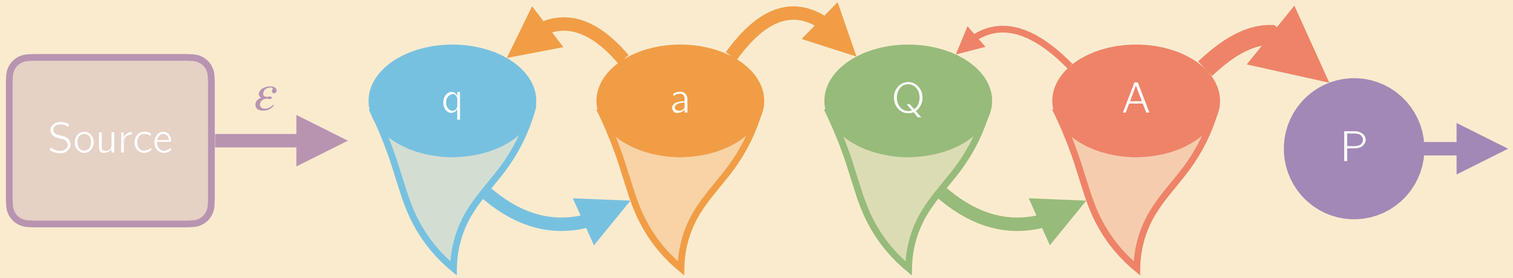
# Modeling the source

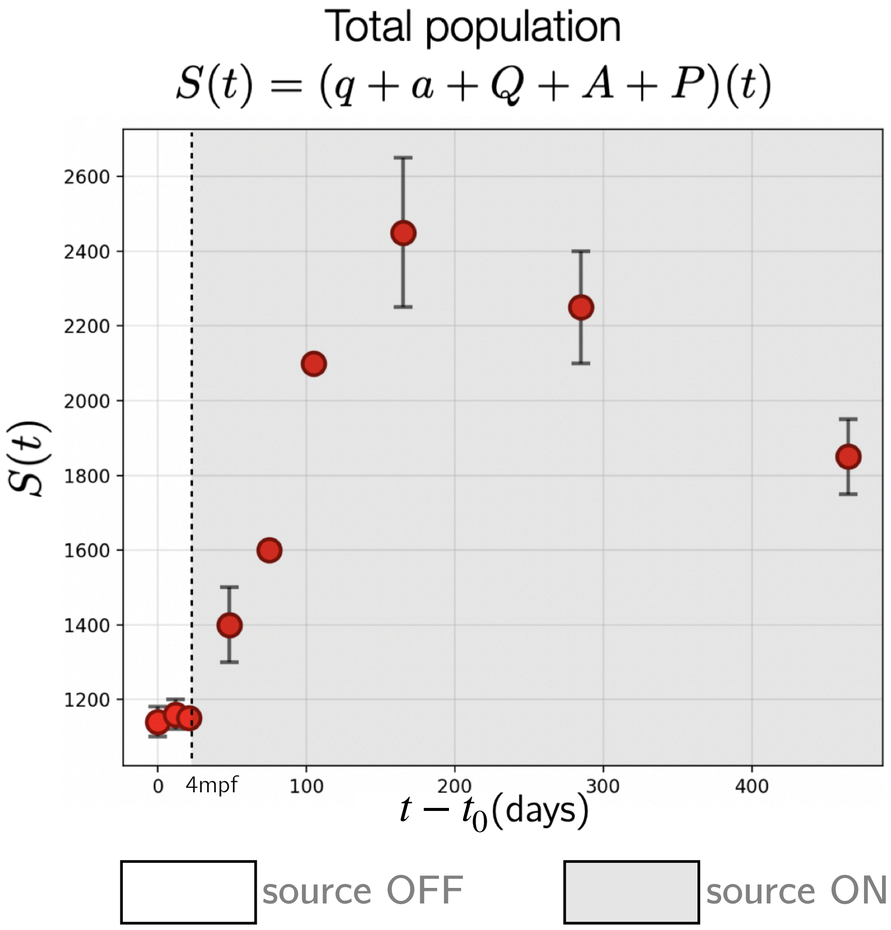
# Investigation: Modeling the source



# Investigation: Modeling the source

**a**. Introduce cells in the population, at the top of the hierarchy, and at a small constant rate $\varepsilon > 0$.

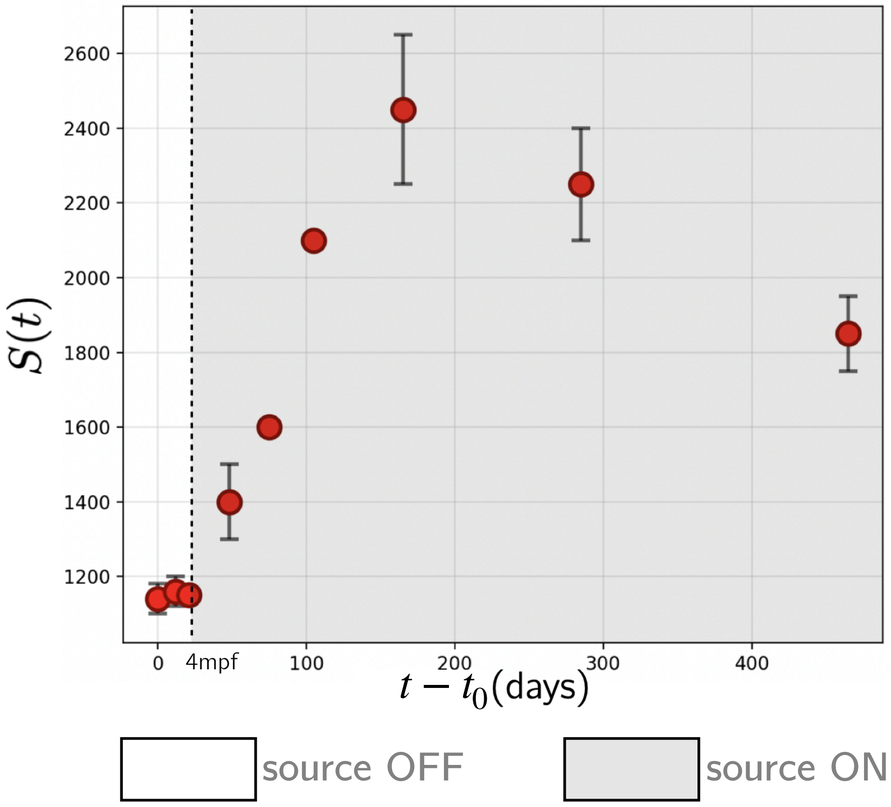


# Investigation: Modeling the source

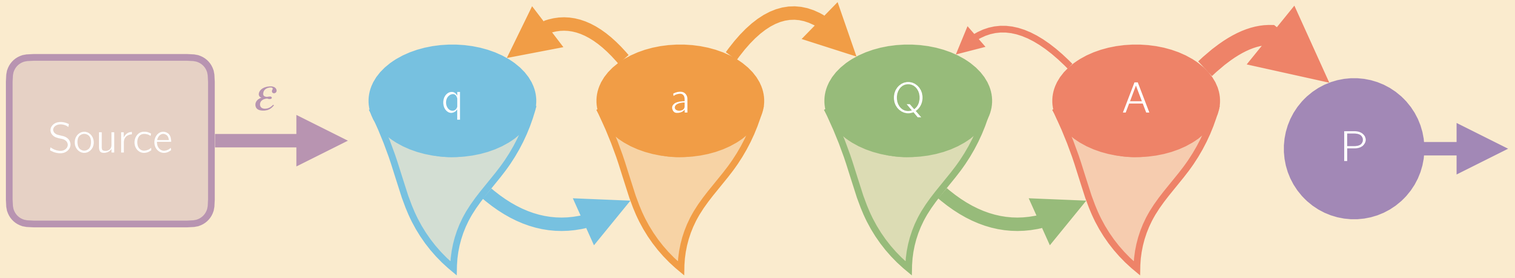
Total population

$S(t) = (q + a + Q + A + P)(t)$

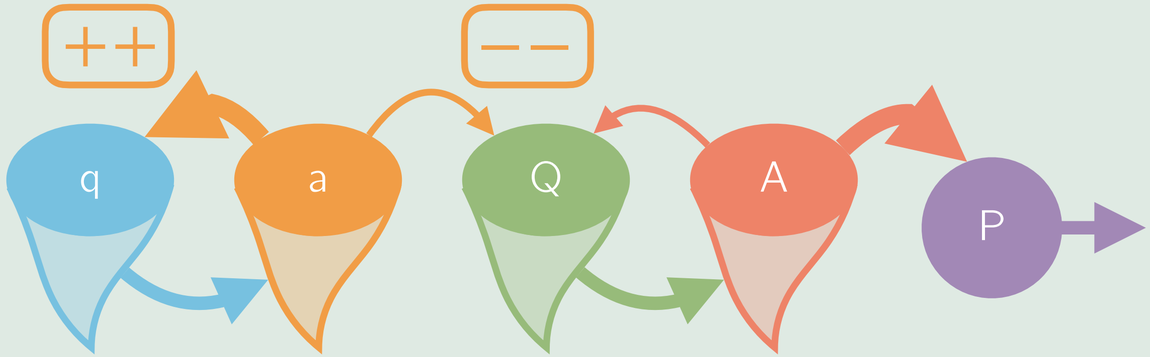



source OFF  source ON

**a**. Introduce cells in the population, at the top of the hierarchy, and at a small constant rate $\varepsilon > 0$.



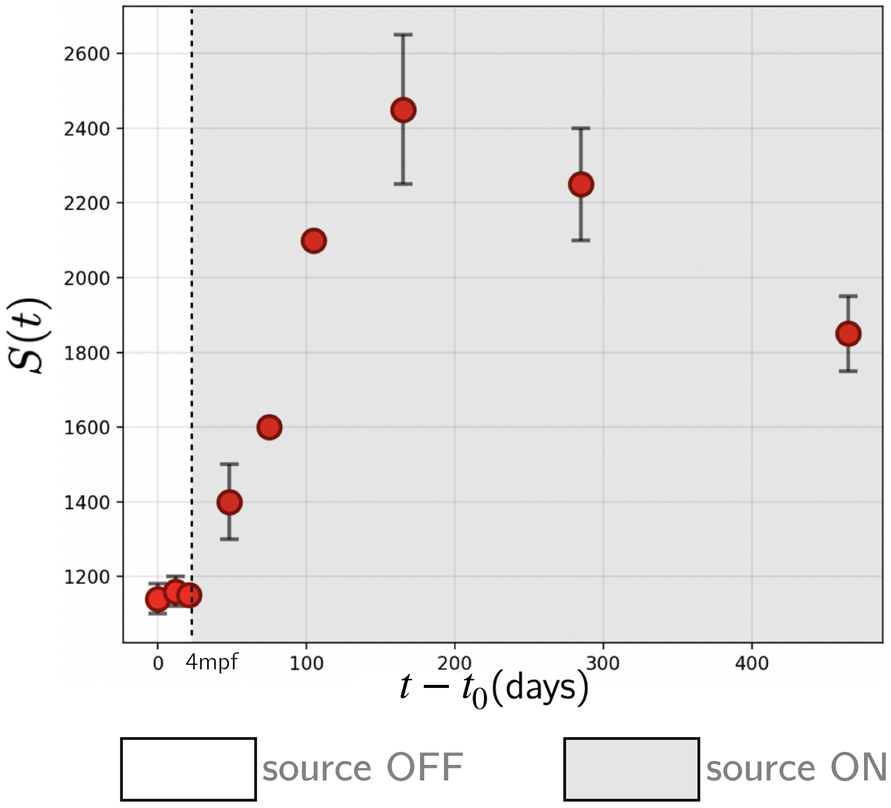

**b**. Slightly increase the self-renewal rate of reservoir aNSCs by$\varepsilon > 0$.



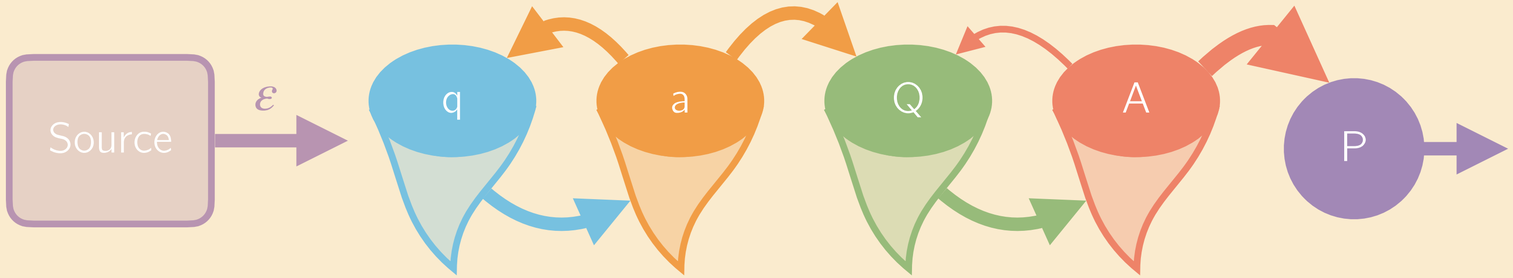
# Investigation: Modeling the source

Total population

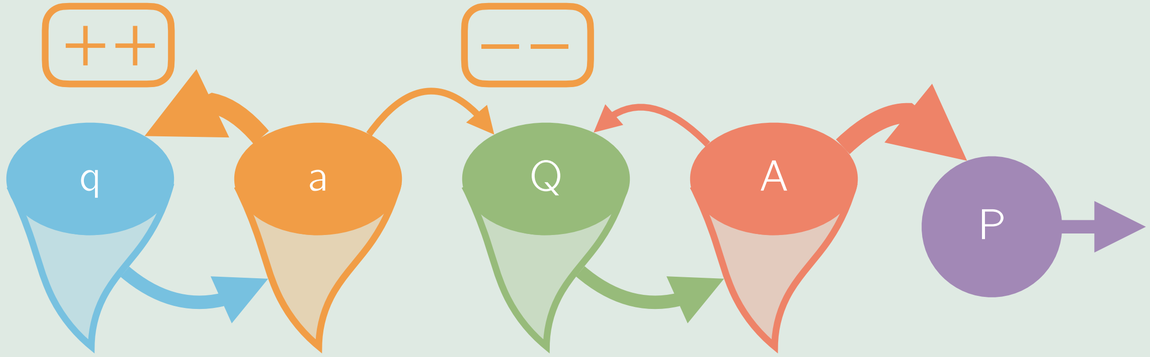
$S(t) = (q + a + Q + A + P)(t)$



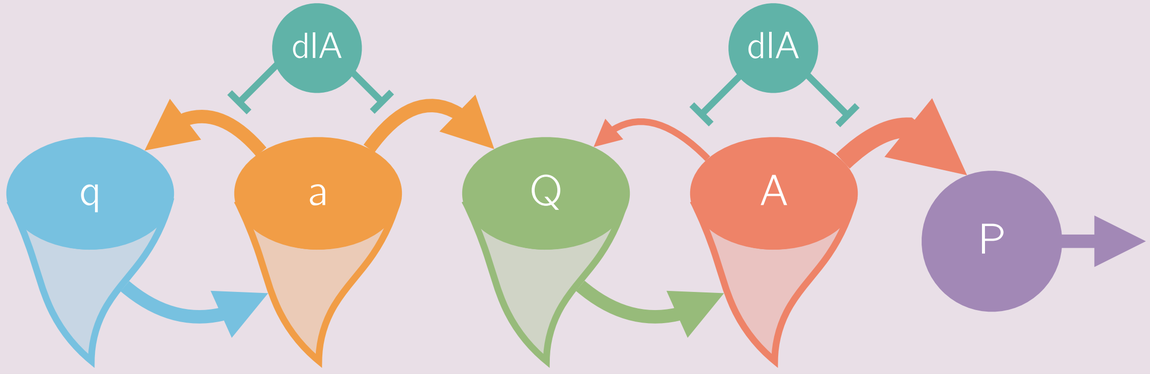

**a**. Introduce cells in the population, at the top of the hierarchy, and at a small constant rate $\varepsilon > 0$.



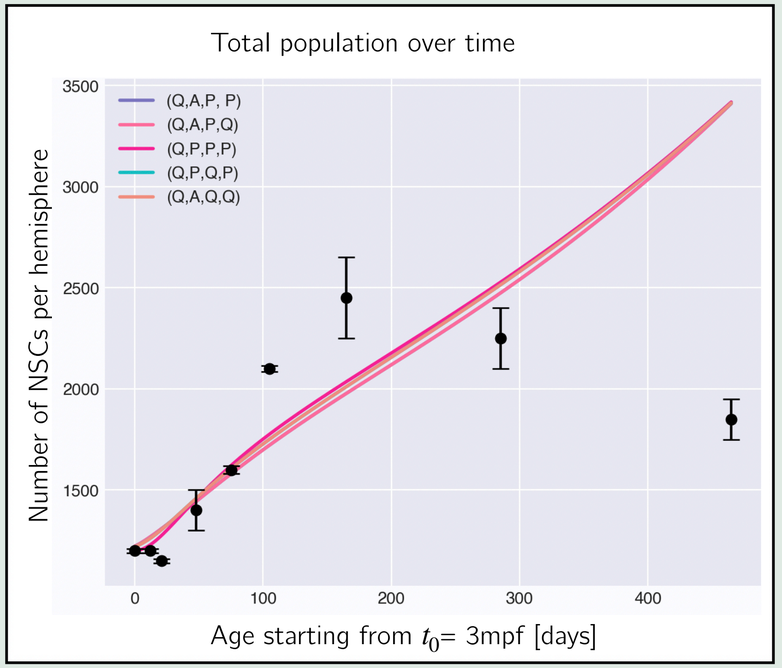

**b**. Slightly increase the self-renewal rate of reservoir aNSCs by$\varepsilon > 0$.

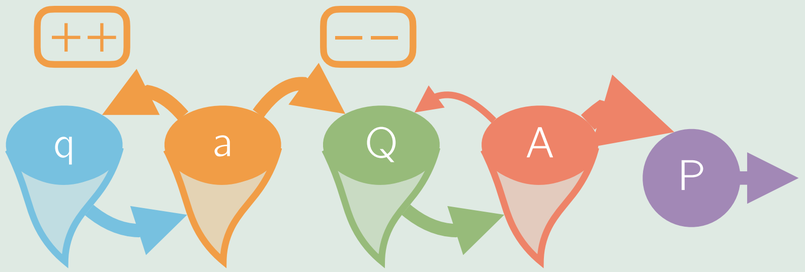



**c**. Notch-Delta signaling controls the self-renewal rate of aNSCs

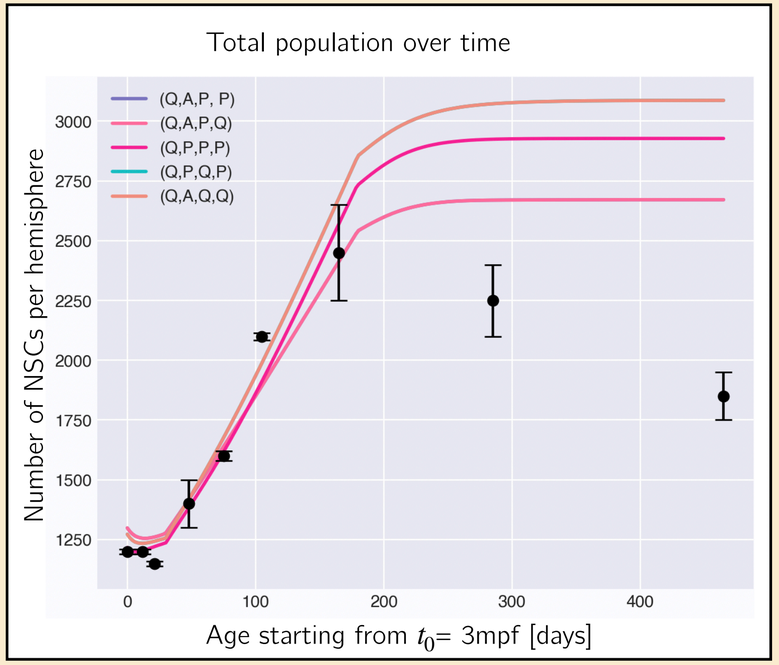


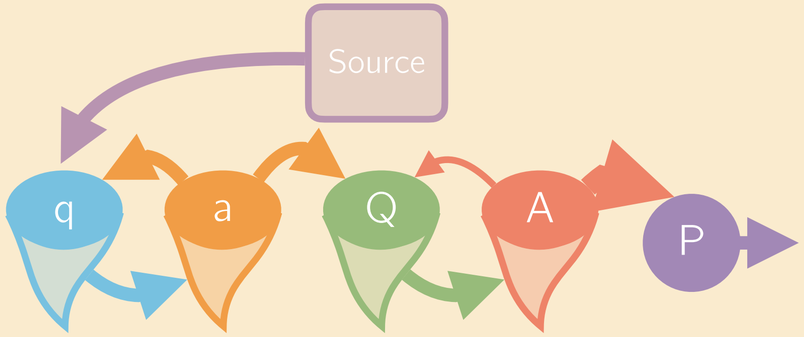
**b**. Slightly increase the self-renewal rate of reservoir aNSCs by $\varepsilon > 0$.



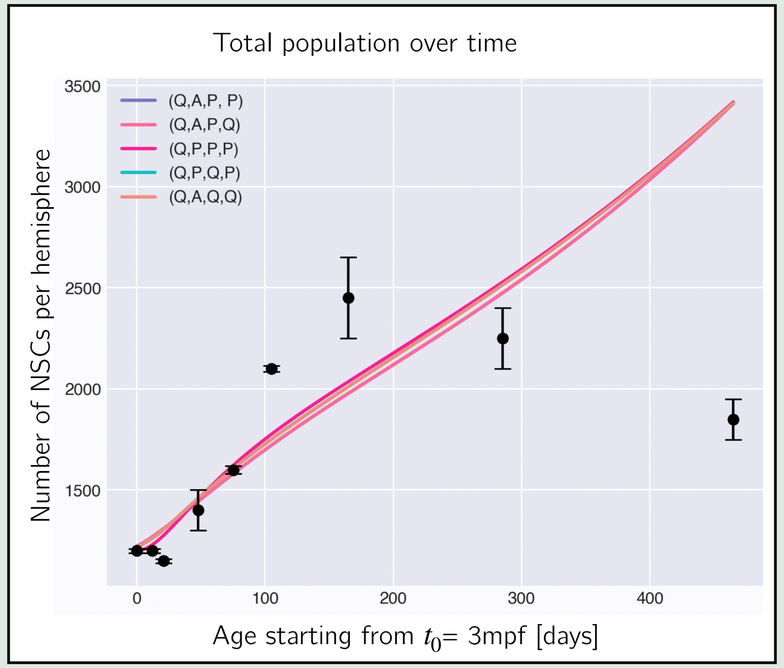



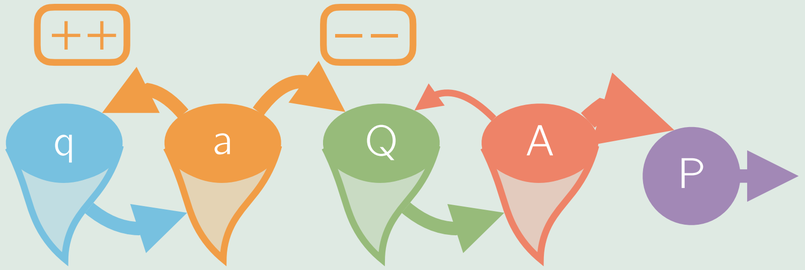
**a**. Introduce cells in the population, at a small constant rate $\varepsilon > 0$.



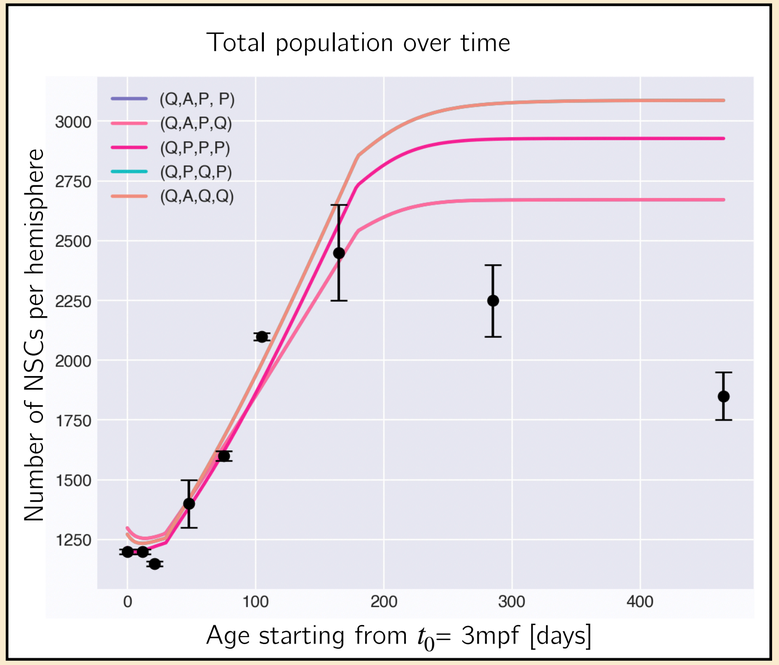



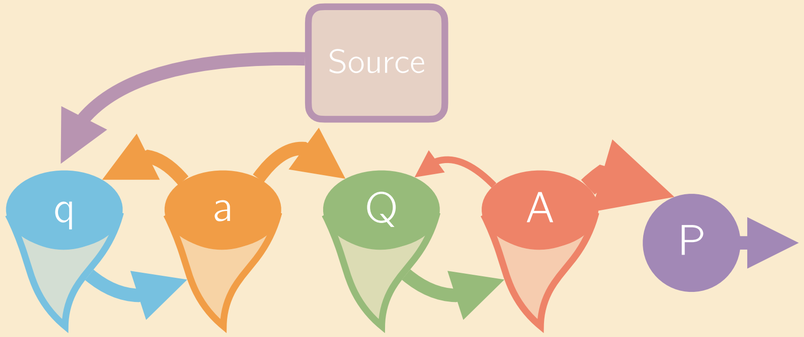

**b**. Slightly increase the self-renewal rate of reservoir aNSCs by $\varepsilon > 0$.



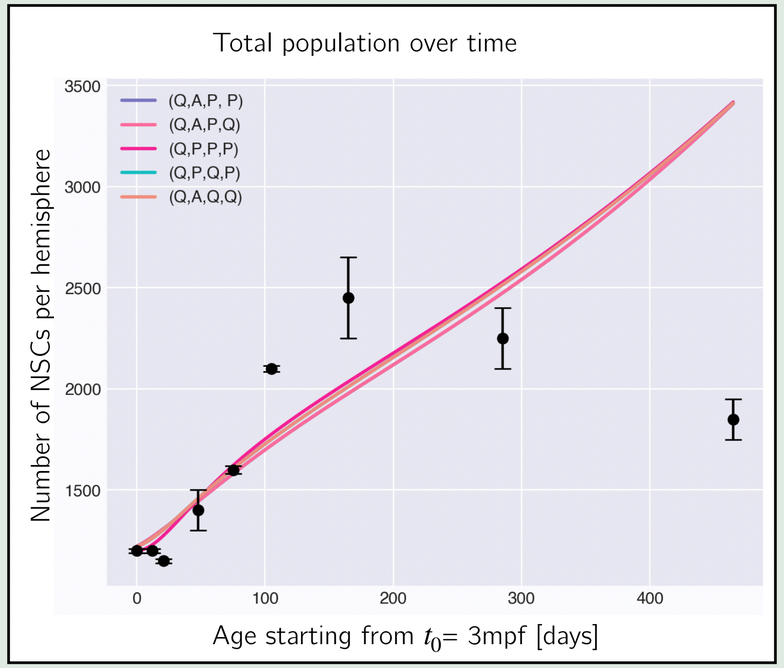



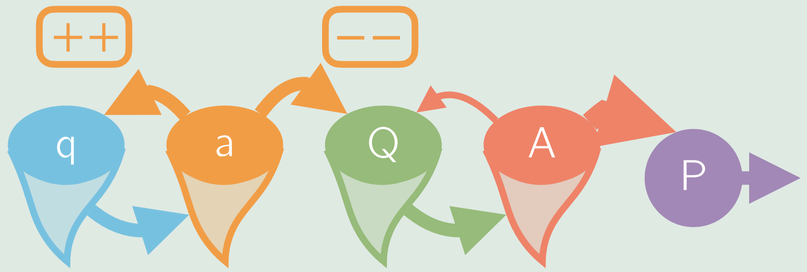
**a**. Introduce cells in the population, at a small constant rate $\varepsilon > 0$.



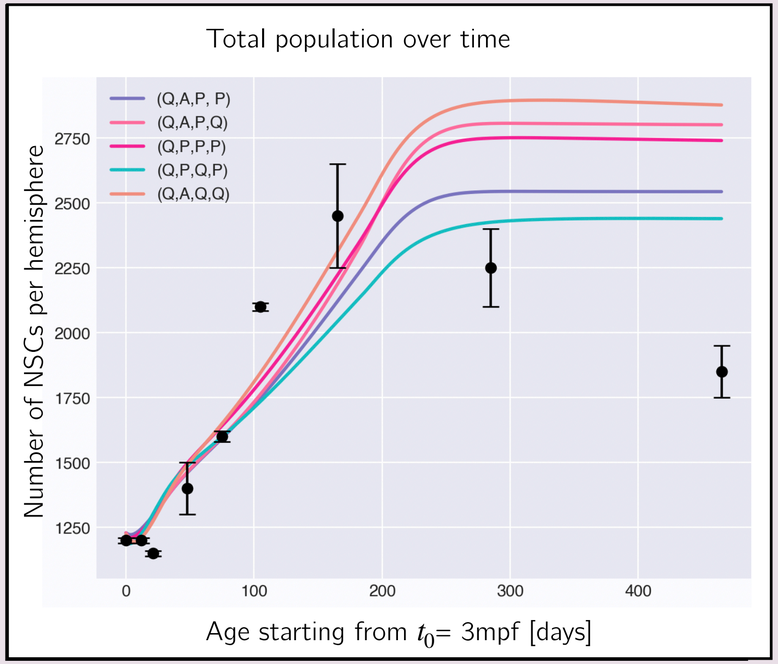



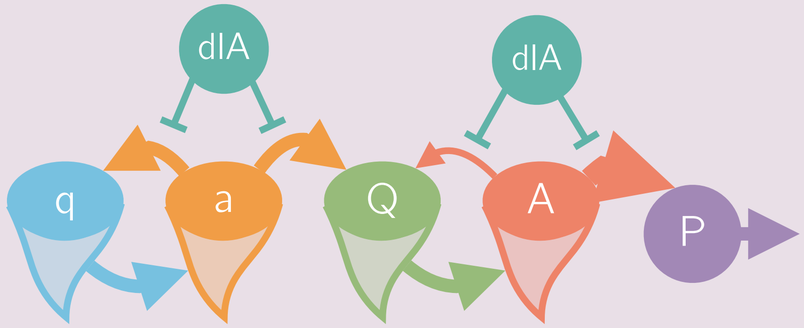

**b**. Slightly increase the self-renewal rate of reservoir aNSCs by $\varepsilon > 0$.



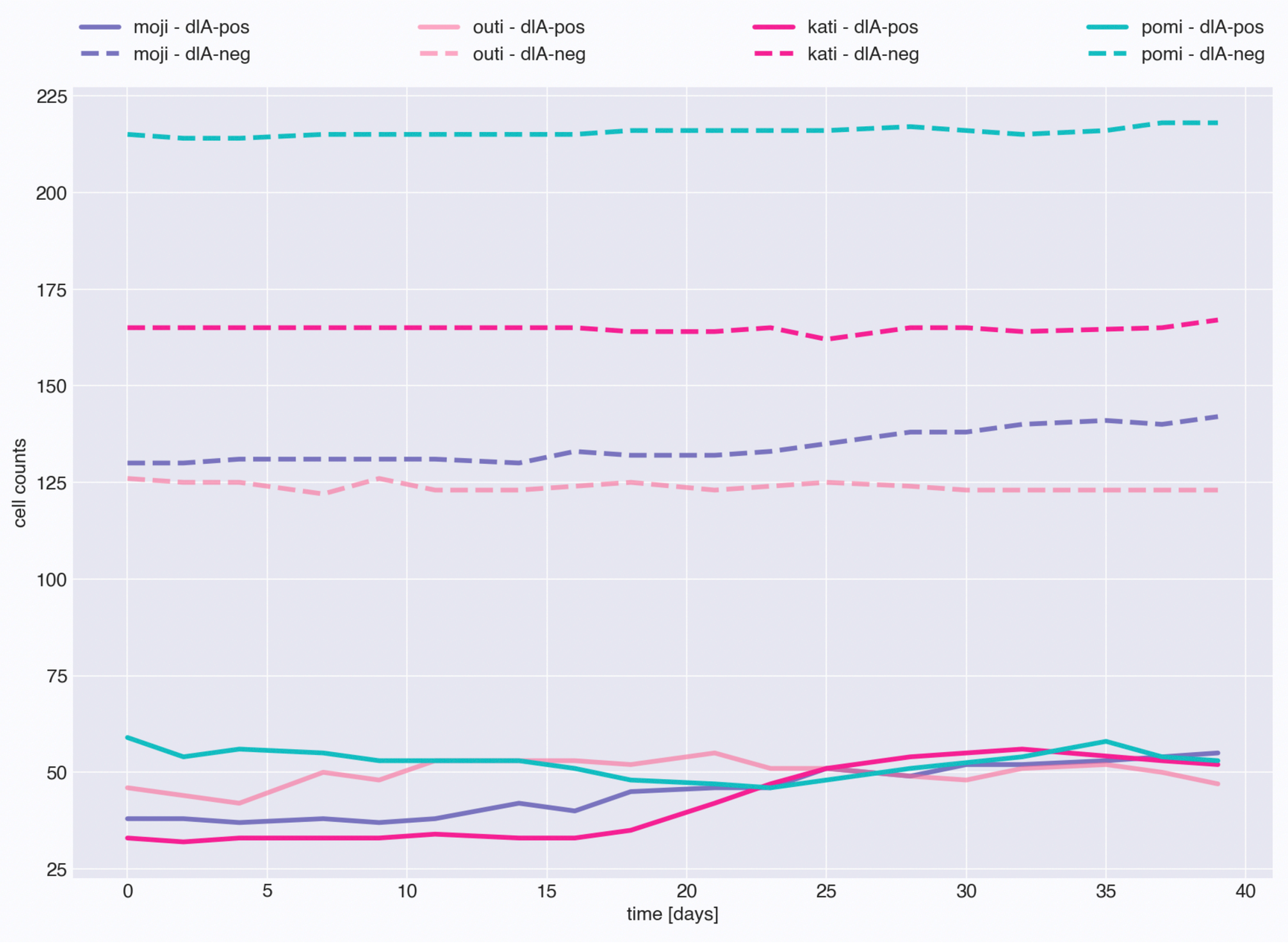

**c**. Notch-Delta signaling controls the self-renewal rate of aNSCs too.



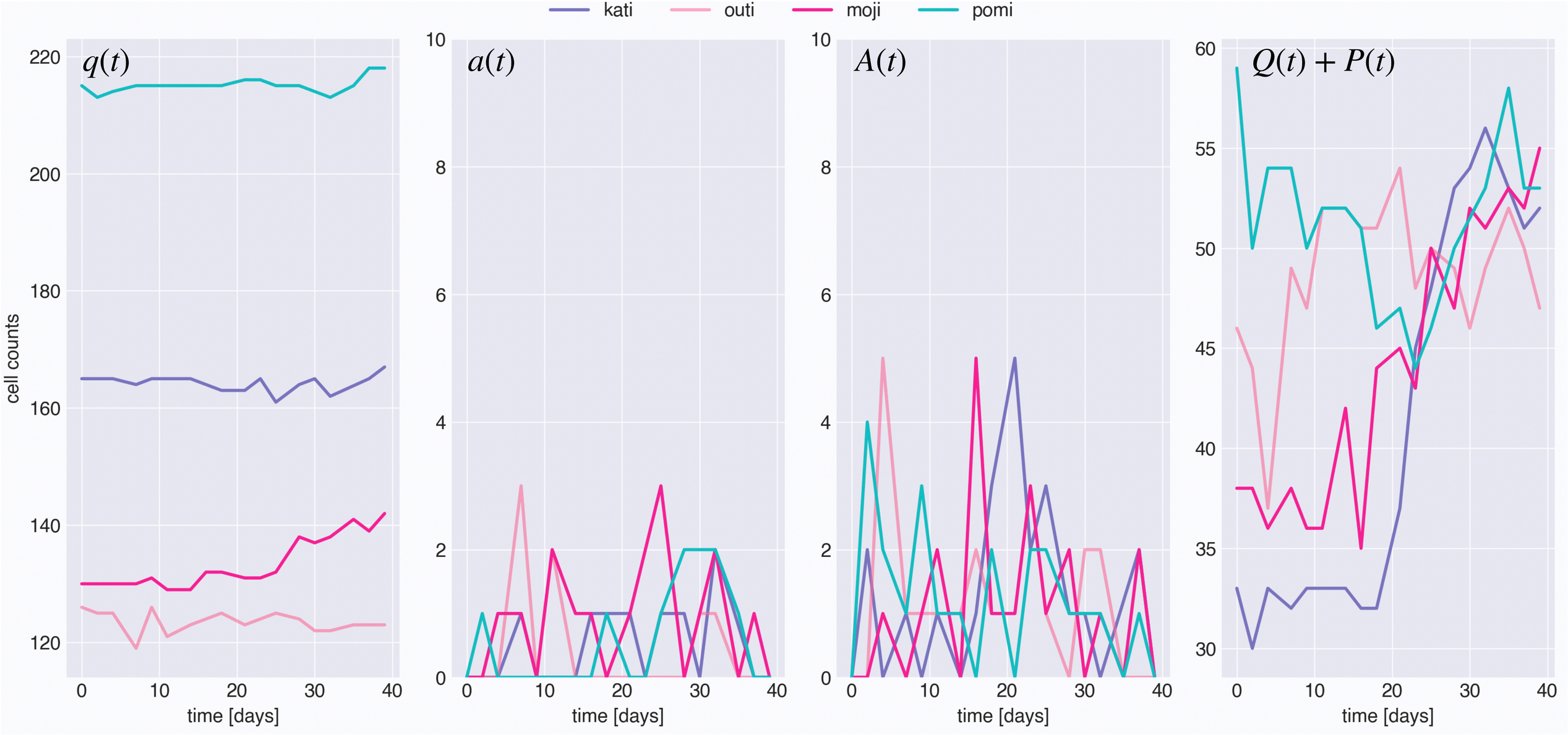



*In vivo* data now available!

# Comparison of deltaA-neg (Reservoir) and deltaA-pos (Operational) cell numbers over time per fish



# Figure (temp): Number of cells of each type over time per fish



Thank you for your attention!