

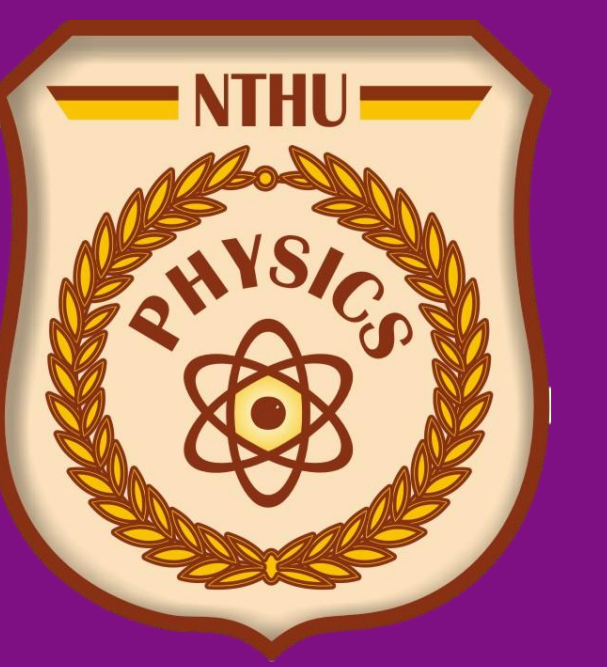


# Modeling Multi-Peak Patterns in Cell Polarity:

The Role of an Intermediate Species' Retention Rate in Reduced Two-Component Activator-Substrate Model

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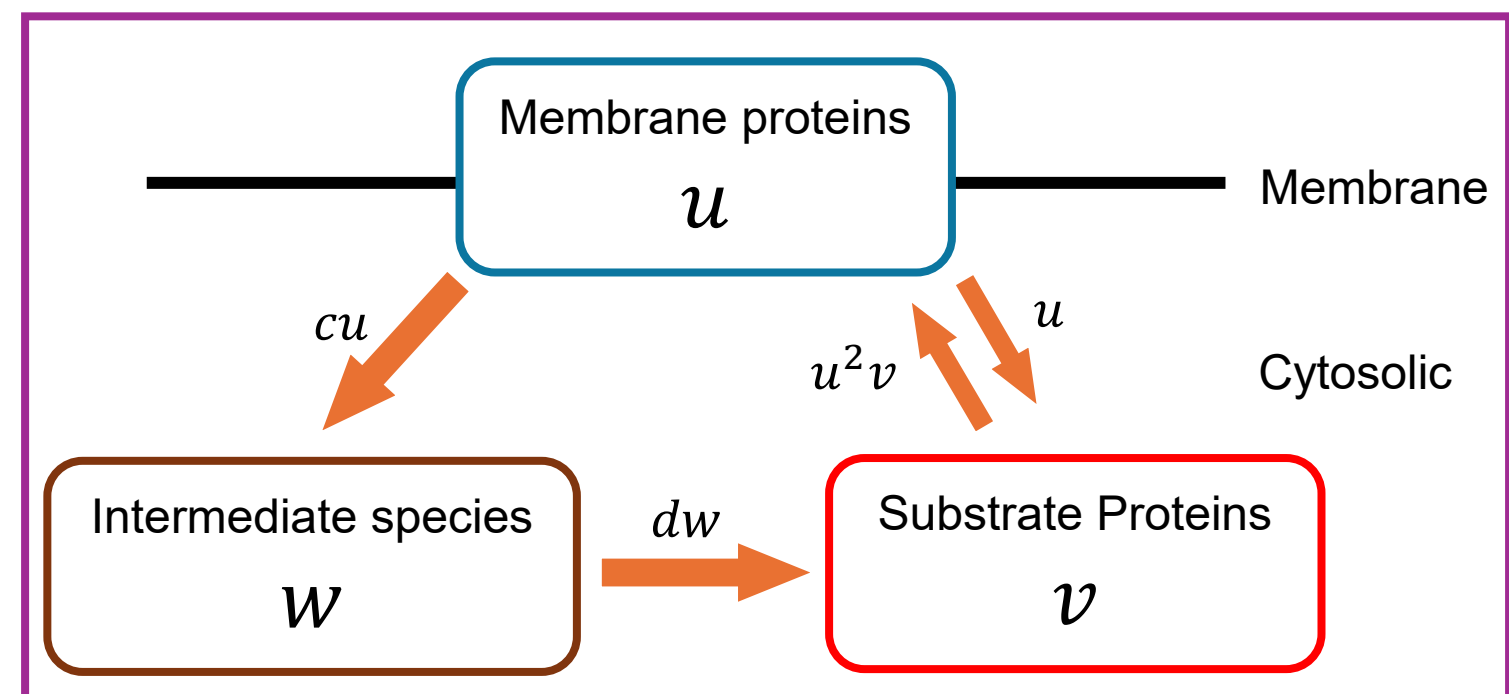
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## Cell Polarity

Cell polarity is a fundamental feature of cell morphology and function. In many cell types, polarity is regulated by conserved protein family, such as GTPases. Experiments have shown that while some cells preferentially form a single polarity domain, others stably maintain multiple polarity domains. Since these distinct behaviors are governed by the same protein family, a key theoretical challenge is to identify a minimal model that can capture both **competition** (single polarity) and **equalization** (multiple polarity) dynamics.

### 3-Species Mass Conserved Activator Substrate (MCAS) Model (Chiou et al., 2021)



$$\begin{aligned} \frac{\partial u}{\partial t} &= u^2v - u - cu + D_u \frac{\partial^2 u}{\partial x^2} \\ \frac{\partial v}{\partial t} &= -u^2v + u + dw + D_v \frac{\partial^2 v}{\partial x^2} \\ \frac{\partial w}{\partial t} &= cu - dw + D_w \frac{\partial^2 w}{\partial x^2} \end{aligned}$$

Figure 1: Schematic diagram of a 3-species MCAS model for cell polarity. Arrows indicate the conversion pathway between each species. Conversion from  $u$  to  $v$  occurs both directly and via the intermediate species  $w$ .

- Membrane Proteins has lower mobility compared to cytosolic species

$$D_u \ll D_v \approx D_w$$

- Parameter  $c$ : conversion coefficient from  $u$  to  $w$ .
- Parameter  $d$ : conversion coefficient from  $w$  to  $v$ .
- In the limiting case  $c = 0$ , the system has been shown by Chiou et al. (2018) to exhibit only single-polarity (competition) dynamics.

## Competition vs Equalization

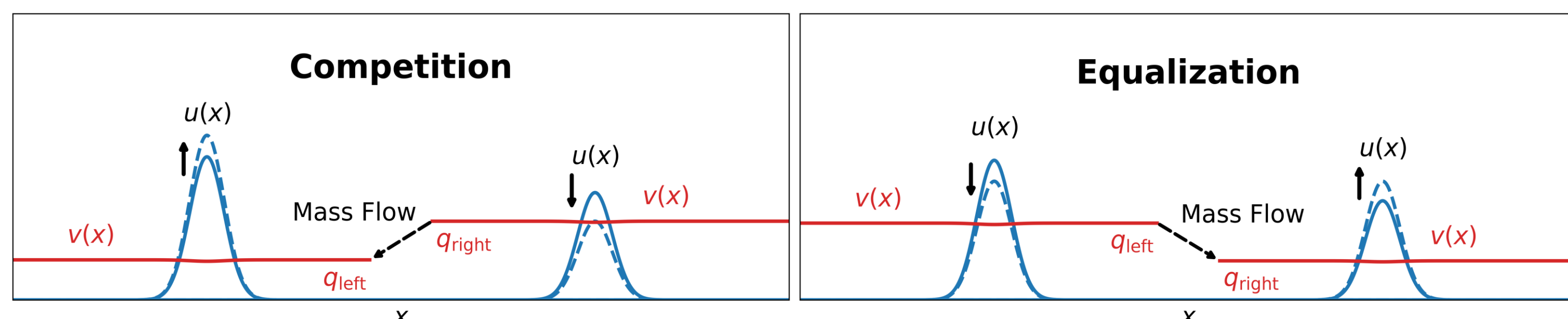
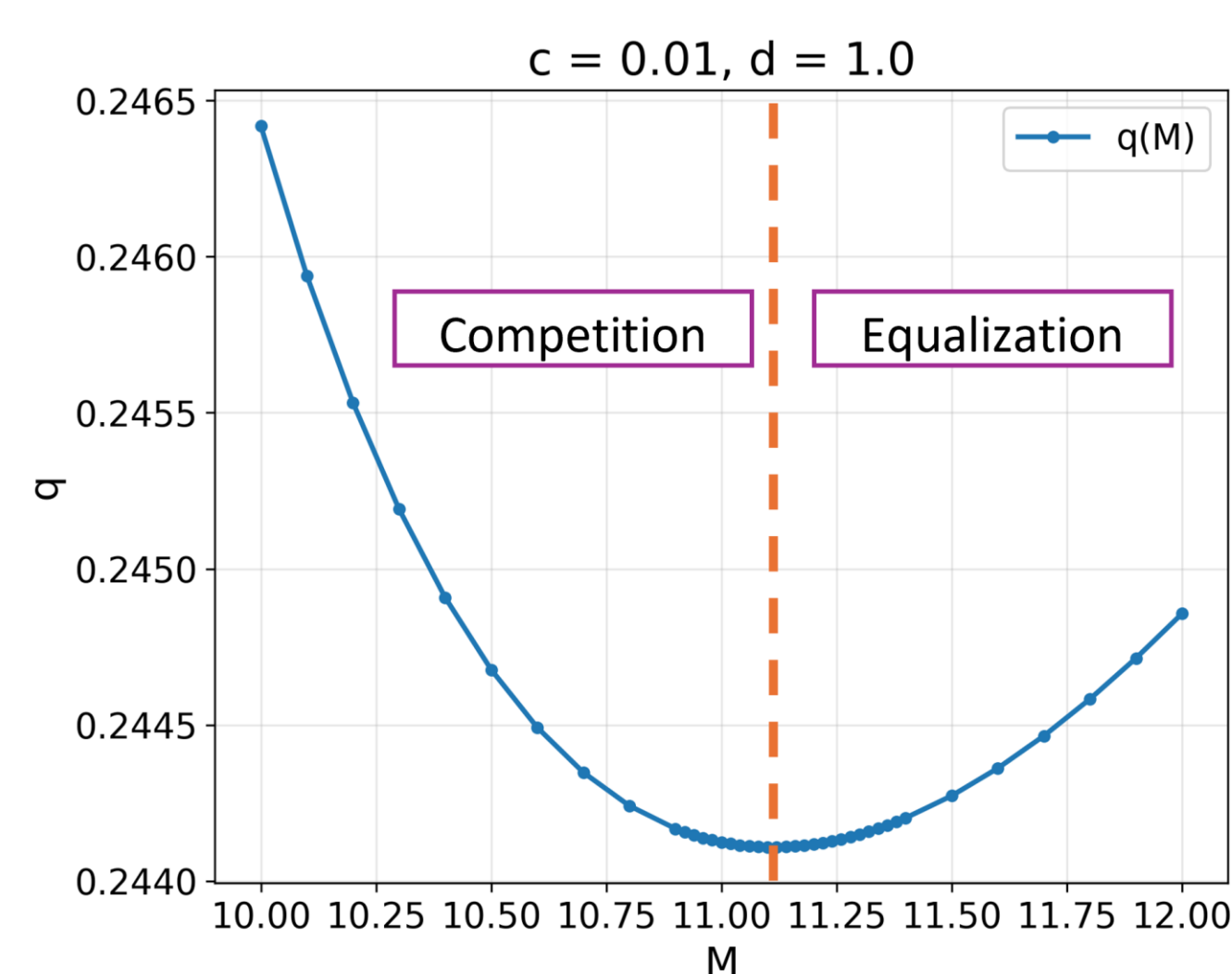


Figure 2: Schematic illustration of polarity site interactions in the competition (left) and the equalization (right) regimes. Localized peaks of the membrane-bound species  $u(x)$  (blue line) interact through the far-field substrate level  $q$  of  $v(x)$  (red line). Differences in  $q$  drive mass flux between sites, determining whether peaks compete (single-polarity outcome) or equalize (multiple polarity of equal size).

- Differences in  $q$  between polarity sites generate directed mass flux, leading to either competition or equalization
- The interaction outcome is determined by how  $q$  depends on local total mass  $M$  of a polarity site.



$$\begin{aligned} \frac{dq}{dM} < 0 &\Rightarrow \text{competition} \\ \frac{dq}{dM} > 0 &\Rightarrow \text{equalization} \end{aligned}$$

Figure 3: Far-field substrate level  $q$  as a function of local total mass  $M$  with  $c = 0.01, d = 1$ . Dashed line marks the transition point where  $dq/dM = 0$ .

- What is the **mechanistic role of the intermediate species** in regulating competition and equalization dynamics?
- How do the conversion coefficient  $c$  and  $d$  regulate transition between competition and equalization?

### Effective 2-Species Model with Source/Sink

Sum up the cytosolic species

$$\text{let } v' = v + w, \text{ since } D_v = D_w$$

$$\frac{\partial v'}{\partial t} = -u^2v' + (1+c)u + u^2w + D_v \frac{\partial^2 v'}{\partial x^2}$$

$$\frac{\partial u}{\partial t} = \underbrace{u^2v'}_{\text{Local Activation}} - \underbrace{(1+c)u}_{\text{Dissociation}} - \underbrace{u^2w}_{\text{Effective Sink}} + D_u \frac{\partial^2 u}{\partial x^2}$$

$$\frac{\partial v'}{\partial t} = -u^2v' + (1+c)u + \underbrace{u^2w}_{\text{Effective Source}} + D_v \frac{\partial^2 v'}{\partial x^2}$$

- $v' = v + w$  represents the whole cytosolic substrate
- The 3-species MCAS model is mathematically equivalent to the 2-species model with an effective source/sink associated with the intermediate species.

## How the presence of Intermediate species allows equalization

Steady states requires:

$$\begin{aligned} v'(x) = v(x) + w(x) &= -\frac{D_u}{D_v}u(x) + q \\ \int_0^{u_{max}} u^2v' - (1+c)u - u^2w \, du &= 0 \end{aligned}$$

Reaction of  $u$

Reaction of  $u$  in steady states

$$F(u, q) = -\frac{D_u}{D_v}u^3 + (q - w(u))u^2 - (1+c)u$$

Without the  $w$ -species ( $c = 0$ )

$$F(u, q) = -\frac{D_u}{D_v}u^3 + qu^2 - u$$

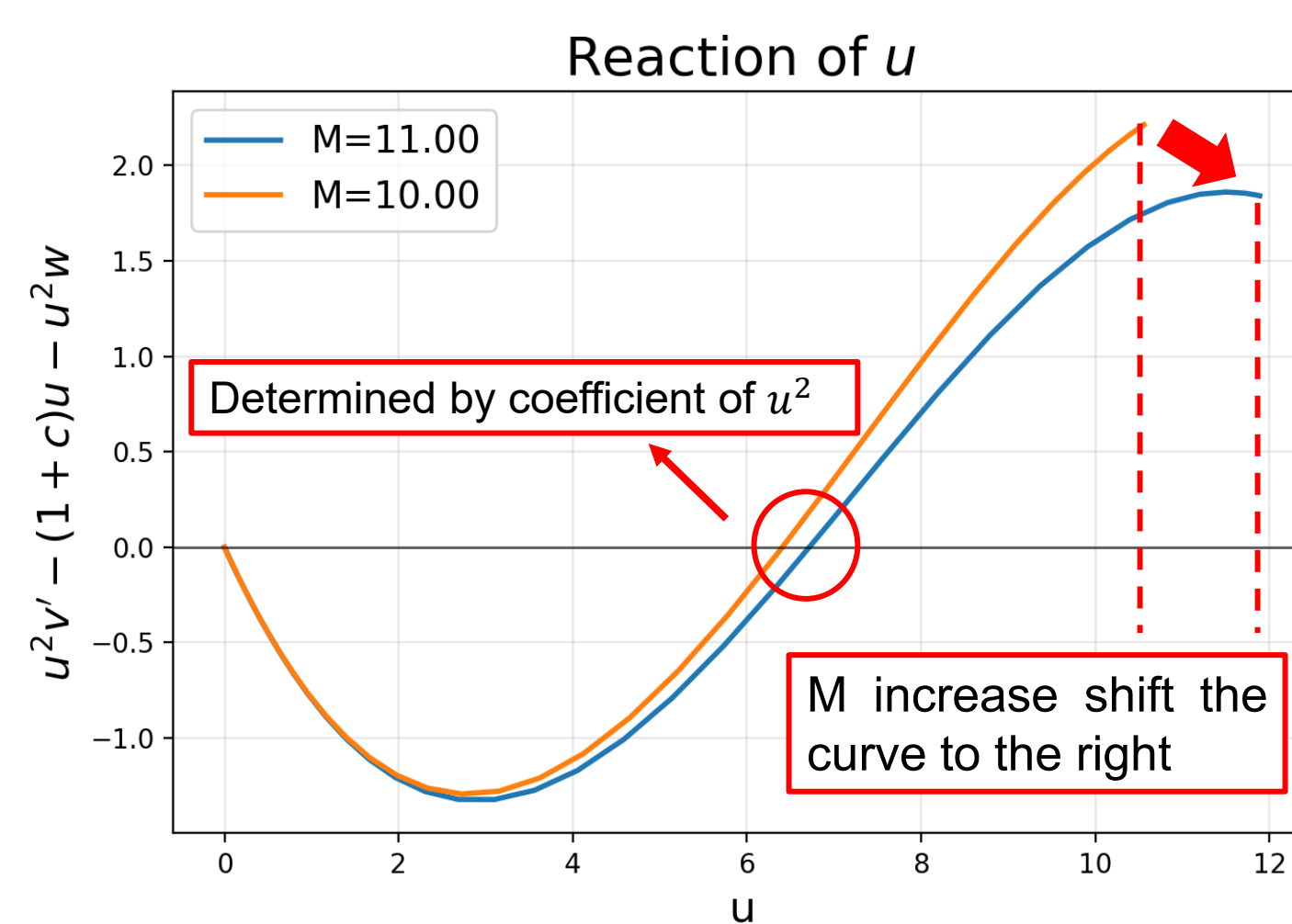


Figure 4: Reaction of  $u$  as a function of  $u$

- Larger  $M$  requires larger  $u_{max}$ .
- This requires a rightward shift of the reaction curve
- The shift is determined by the coefficient of  $u^2$ , namely  $q$
- Thus, increasing  $M$  requires a decrease in  $q$
- Therefore, equalization cannot occur without  $w$ -species.

With  $w$ -species ( $c > 0$ )

- The coefficient of  $u^2$  becomes  $(q - w(u))$
- The control constant is no longer  $q$  alone
- We define an effective coefficient

$$(q - w)_{eff} = q - \frac{\int_0^{u_{max}} wu^2 \, du}{\int_0^{u_{max}} u^2 \, du}$$

- Hence, increasing  $q$  does not necessarily shift the reaction curve upward
- Instead, equalization is possible since  $q$  and the effective coefficient of  $u^2$  are no longer required to vary in the same direction

## How Do Conversion Coefficients $c$ and $d$ Affect Cell Polarity?

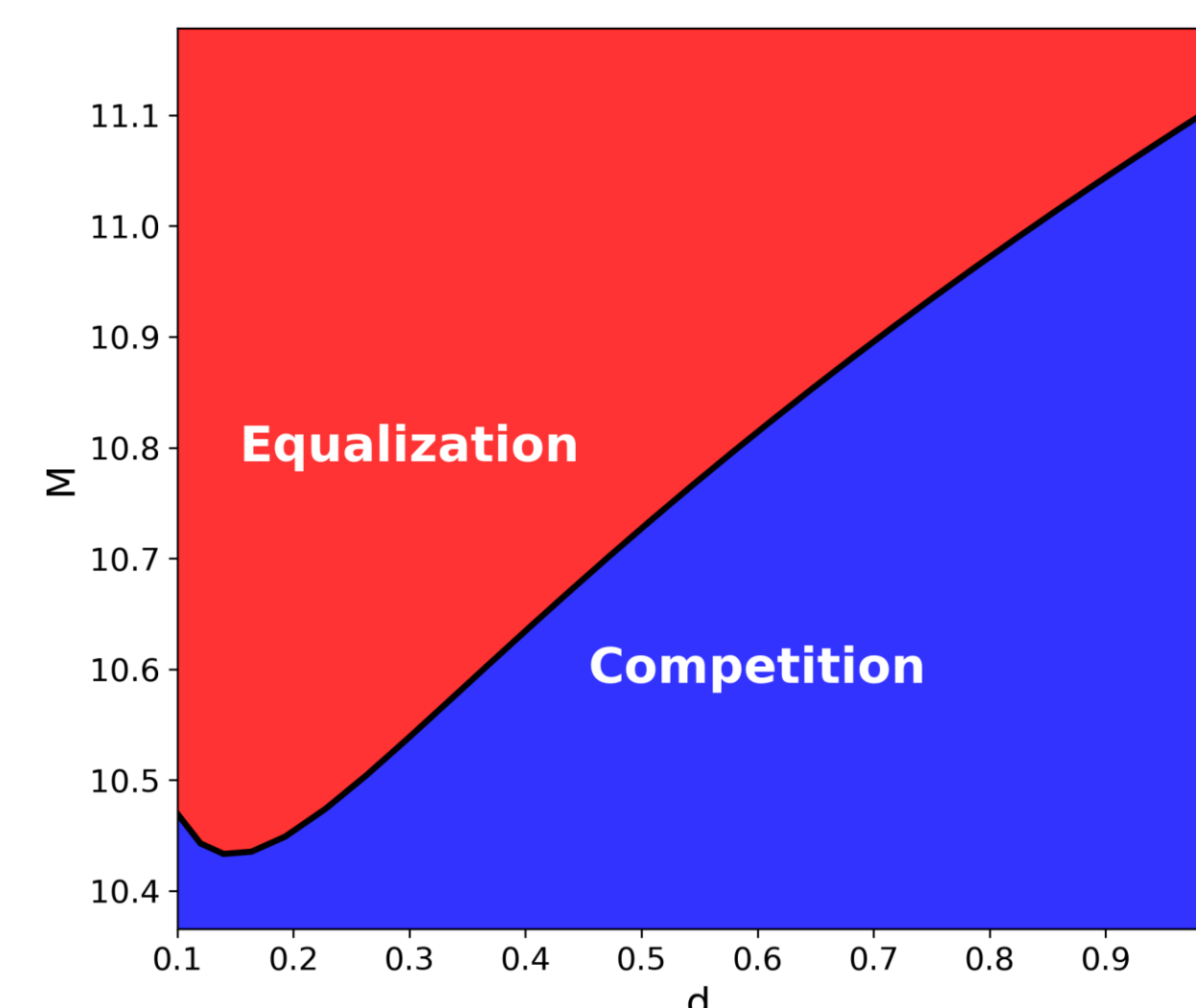


Figure 5: Phase diagram in the  $(d, M)$  plane,  $c = 0.01$ .

- Decrease in  $d$  restrict the conversion of  $w$  into  $v$ , which will reduce the effective supply of  $v$  available to the activator  $u$
- Consequently, the ability of  $u$  to deplete  $v$  weakened, promoting equalization

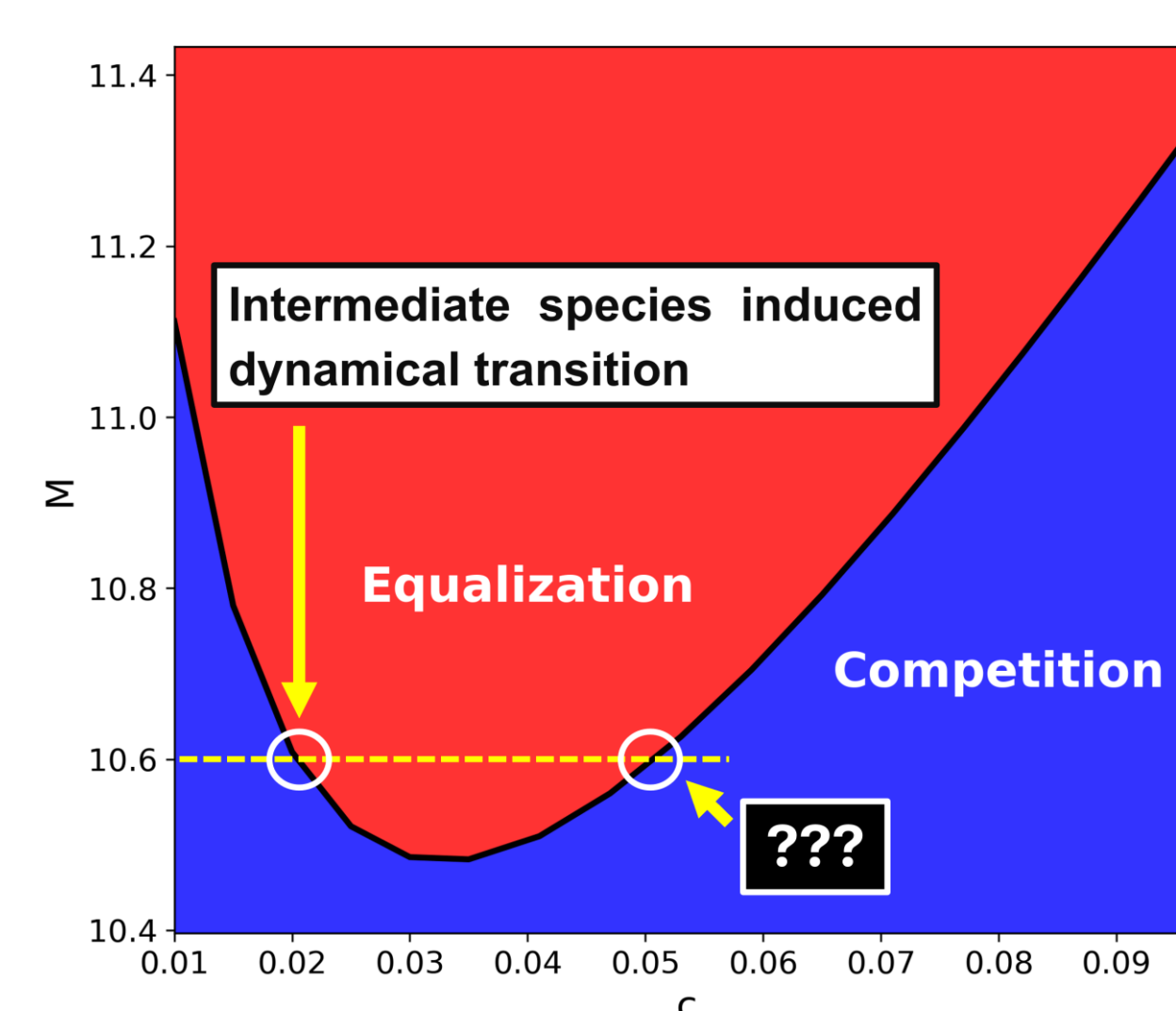


Figure 6: Phase diagram in the  $(c, M)$  plane,  $d = 1.0$

- Increasing  $c$  initially convert more  $u$  to  $w$ , promotes equalization
- At large  $c$  more  $v$  and  $w$  accumulate in the  $u$ -peak region
- $u$  species can consume more substrate as mass redistribution is triggered by the inflow of additional mass.
- Hence the system get back to competition.

## Summary & Future Work

- The intermediate species appear to be an effective sink term to the membrane-bound activator ( $u$ -species), which impedes the growth of  $u$ .
- The presence of intermediate species enable equalization.
- Decreasing the conversion coefficient from  $w$  to  $v$  (that is,  $d$ ) reduces the effective supply of  $v$  to the activator  $u$ , hence promotes equalization.
- Increasing the conversion coefficient from  $u$  to  $w$  (that is,  $c$ ) initially promotes equalization by introducing the intermediate species  $w$ .
- More interestingly, at large  $c$ , the system re-enters the competition regime. However, the underlying mechanism remains unclear.