QUORUM SENSING

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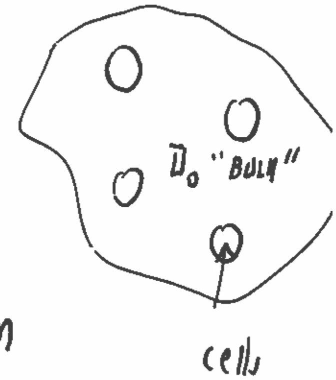
Q1

CONSIDER THE COUPLED ODE SYSTEM,

$$\frac{dU_0}{dt} = -U_0 - \frac{\rho}{m}\sum_{j=1}^{m}\left(U_0 - V_j\right)$$



SELKOV KINETICS

$$\frac{dV_j}{dt} = \alpha W_j + W_j V_j^2 - V_j + \left(U - V_j\right) \qquad j = 1, \ldots, m$$

$$\frac{dW_j}{dt} = \beta\left(\mu - \left(\alpha W_j + W_j V_j^2\right)\right)$$

HERE $\alpha \geq 0$, $\mu \geq 0$, $\beta > 0$ ARE PARAMETERS, m IS THE NUMBER OF "CELLS" AND ρ MEASURES THE COUPLING OF THE CELL DYNAMICS (V_j, W_j) TO THE "MEAN-FIELD" U_0.

Q1: SUPPOSE $\rho = 0$ FOR UNCOUPLED CELLS. FOR A FIXED $\beta = 0.25$ FIND AND PLOT THE REGION IN THE α VERSUS μ PARAMETER PLANE WHERE CELLULAR OSCILLATIONS CAN OCCUR, AND WHERE THE STEADY-STATE IS STABLE.

Q2: IF WE VARY α IN TIME CAN WE CREATE OSCILLATIONS THROUGH A DELAYED BIFURCATION?

Q3: SUPPOSE THAT $\rho > 0$. FIND A STEADY-STATE SOLUTION FOR THE FULL COUPLED SYSTEM WITH IDENTICAL CELLS (i.e. $V_j = V$, $W_j = W$ $\forall j$).

Q4 DOES THE STRENGTH OF THE COUPLING ACT TO TRIGGER NEW OSCILLATIONS?

A1: WE CONSIDER FIRST A SINGLE CELL. WE IGNORE j SUBSCRIPT AND WE WRITE

$$\frac{dv}{dt} = f(v,w) = \alpha w + w v^2 - v$$

$$\frac{dw}{dt} = g(v,w) = \beta(\mu - (\alpha w + w v^2)).$$

THE STEADY-STATE HAS $v = \alpha w + w v^2 = \mu$ SO THAT

$$v_e = \mu, \quad w_e = \frac{\mu}{\alpha + v_e^2} = \frac{\mu}{\alpha + \mu^2}.$$

NOW WE CALCULATE

$$J = \begin{pmatrix} f_v & f_w \\ g_v & g_w \end{pmatrix} = \begin{pmatrix} 2wv - 1 & \alpha + v^2 \\ -2\beta w v & -\beta(\alpha + v^2) \end{pmatrix}\Bigg|_{\substack{v = v_e \\ w = w_e}}$$

SO

$$\operatorname{tr} J = 2 w_e v_e - 1 - \beta(\alpha + v_e^2)$$

$$\det J = -\beta(2 w_e v_e - 1)(\alpha + v_e^2) + 2\beta w_e v_e (\alpha + v_e^2)$$

$$= \beta(\alpha + v_e^2)$$

IN THIS WAY WE OBTAIN

$$\operatorname{tr} J = \frac{2\mu^2}{\alpha + \mu^2} - 1 - \beta(\alpha + \mu^2)$$

$$\det J = \beta(\alpha + \mu^2)$$

SINCE $\det J > 0$ WE OBTAIN THAT WE HAVE STABILITY IFF $\operatorname{tr} J < 0$. THIS MEANS THAT

$$\frac{2\mu^2}{\alpha + \mu^2} - 1 - \beta(\alpha + \mu^2) < 0 \qquad (*)$$

NOW THE HB BOUNDARY IS WHERE $2\mu^2 = \alpha + \mu^2 + \beta(\alpha + \mu^2)^2$.

SET $z = \alpha + \mu^2 \longrightarrow \beta z^2 + z - 2\mu^2 = 0$ SO

$$z = \alpha + \mu^2 = \frac{-1 \pm \sqrt{1 + 8\mu^2 \beta}}{2\beta}.$$

SINCE $\alpha + \mu^2 > 0$ WE MUST TAKE + ROOT SO THAT

$$\alpha_{HB} = -\mu^2 + \left[\frac{-1 + \sqrt{1 + 8\mu^2 B}}{2B}\right].$$

NOW IF $B = .25$ WE GET

$$\alpha_{HB} = -\mu^2 + 2\left[-1 + \sqrt{1 + 2\mu^2}\right].$$

OBSERVE THAT $\alpha_{HB} = 0$ WHEN $\mu = 0$ AND $\mu = 2$. LET $\zeta = \mu^2$

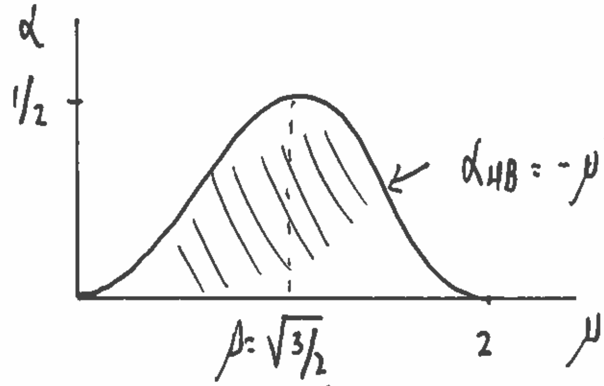
SO THAT $\dfrac{\partial \alpha_{HB}}{\partial \zeta} = -1 + \dfrac{2}{\sqrt{1+2\zeta}}\left(\dfrac{1}{2}\cdot 2\right) = 0$ WHEN $\sqrt{1+2\zeta} = 2 \rightarrow 1 + 2\zeta = 4$

SO $\zeta = 3/2$.

THUS α_{HB} IS MAXIMIZED WHEN $\mu = \sqrt{3/2}$.

$$\alpha_{HB\,MAX} = -\frac{3}{2} + 2\left[-1 + \sqrt{1+3}\right] = -\frac{3}{2} + 2(-1+2) =$$

THE PLOT IS

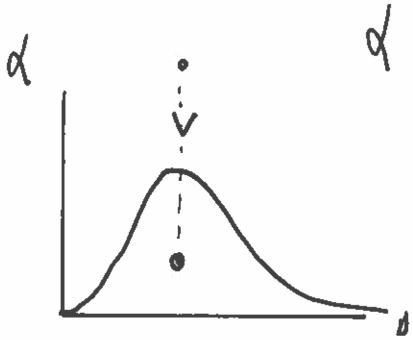


$\alpha_{HB} = -\mu^2 + 2\left[-1 + \sqrt{1+2\mu^2}\right].$

INSIDE SHADED REGION: $\det J > 0$, $\operatorname{tr} J > 0$ (V_e, W_e) IS UNSTABLE FIXED POINT AND $\exists$ PERIODIC OSCILLATIONS FOR A SINGLE CELL

OUTSIDE SHADED REGION: THE FIXED POINT (V_e, W_e) IS LINEARLY STABLE

Q2: NOW SUPPOSE WE TAKE $\mu = \sqrt{3/2}$ AND VARY α SLOWLY IN TIME AS



$$\alpha = \begin{cases} .75 - .005t & \text{FOR } 0 \le t \le 100 \\ .25 & \text{FOR } t > 100 \end{cases}$$

THE PATH IS AS SHOWN.

WILL WE OBSERVE A DELAYED HB?

Q4

FOR A DELAYED-BIFURCATION ANALYSIS WE PUT

$$\begin{pmatrix} V \\ W \end{pmatrix} = \begin{pmatrix} V_e \\ W_e \end{pmatrix} + \underset{\sim}{c}\, e^{\Phi(\tau)/\varepsilon} \quad \text{WITH} \quad \tau = \varepsilon t \qquad \varepsilon = .005.$$

INTO $\quad \varepsilon\, dv/d\tau = f(v,w)\,, \quad \varepsilon\, dw/d\tau = g(v,w) \quad$ WITH $\quad \alpha = .75 - \varepsilon t$

WE OBTAIN

$$\dot{\Phi}^2 - \operatorname{tr} J\, \dot{\Phi} + \det J = 0.$$

BUT

$$\dot{\Phi} = \frac{\operatorname{tr} J \pm \sqrt{(\operatorname{tr} J)^2 - 4\det J}}{2}$$

WHERE WITH $B = 1/4$ WE OBTAIN THAT (WITH $p = \sqrt{3/2}$)

$$\operatorname{tr} J = \frac{2p^2}{\alpha + p^2} - 1 - B(\alpha + p^2) = \frac{3}{\alpha + 3/2} - 1 - \frac{1}{4}\left(\alpha + \frac{3}{2}\right)$$

$$= \frac{6}{2\alpha+3} - 1 - \frac{1}{8}(2\alpha+3) = \frac{1}{(2\alpha+3)}\left[6 - (2\alpha+3) - \frac{1}{8}(2\alpha+3)^2\right]$$

$$\det J = B(\alpha + p^2) = \frac{1}{4}\left(\alpha + \frac{3}{2}\right) = \frac{1}{8}(2\alpha+3)$$

SO

$$(\operatorname{tr} J)^2 - 4\det J = \frac{1}{(2\alpha+3)^2}\left[6 - (2\alpha+3) - \frac{1}{8}(2\alpha+3)^2\right]^2 - \frac{4}{8}(2\alpha+3)$$

$$= \frac{1}{(2\alpha+3)^2}\left(\left[6 - (2\alpha+3) - \frac{1}{8}(2\alpha+3)^2\right]^2 - \frac{1}{2}(2\alpha+3)^2\right].$$

NOW SINCE $.25 < \alpha < .75$ WE LET $X = 2\alpha + 3 \longrightarrow 3.5 < X < 4.5$ AND LET $\tilde{f}(X) = \left[6 - X - \frac{1}{8}X^2\right]^2 - \frac{1}{2}X^2$ ON $3.5 < X < 4.5$. IT IS EASY TO CHECK THAT $\hat{f}(X) < 0$ ON $3.5 < X < 4.5$.

SO $\quad (\operatorname{tr} J)^2 - 4\det J < 0 \quad$ ON THE SWEEP IN α.

HENCE

$$\dot{\Phi} = \frac{\operatorname{tr} J \pm i\sqrt{4\det J - (\operatorname{tr} J)^2}}{2}.$$

THIS MEANS THAT

$$\mathrm{RE}[\dot{\Phi}] = \frac{\mathrm{tr}J}{2}, \quad \text{ON THE SWEEP IN } \alpha.$$

SETTING $\Phi(0) = 0$ WE CONCLUDE THAT A HB WILL BE INITIATED AT THE TIME τ_F FOR WHICH

$$\mathrm{RE}\ \Phi = \frac{1}{2}\int_0^{\tau_F} (\mathrm{tr}\,J(\tau))\,d\tau = 0 \quad \text{WHERE} \quad \mathrm{tr}\,J = \frac{6}{2\alpha+3} - 1 - \frac{1}{8}(2\alpha+3)$$

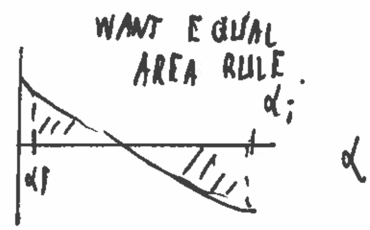
WITH $\alpha = \alpha_i - \tau$.

NOW CHANGE VARIABLES. LET $d\alpha/d\tau = -1$ AND $\alpha_i = .75$, $\alpha_F = \alpha_i - \tau_F$.

THEN WE SEEK $\alpha_F < \alpha_i$ FOR WHICH

$$\mathrm{RE}\ \Phi = \frac{1}{2}\int_{\alpha_i}^{\alpha_F} \mathrm{tr}\,J(\alpha)\,\frac{d\tau}{d\alpha}\,d\alpha = 0 = \frac{1}{2}\int_{\alpha_F}^{\alpha_i} (\mathrm{tr}\,J)\,d\alpha = 0.$$

NOW WE SIMPLY INTEGRATE:



$$\mathrm{RE}\ \Phi = \frac{1}{2}\int_{\alpha_F}^{\alpha_i}\left(\frac{6}{2\alpha+3} - 1 - \frac{1}{8}(2\alpha+3)\right)d\alpha$$

$$= \frac{1}{2}\left[\,3\log(2\alpha+3)\Big|_{\alpha_F}^{\alpha_i} - (\alpha_i - \alpha_F) - \frac{1}{32}(2\alpha+3)^2\Big|_{\alpha_F}^{\alpha_i}\right]$$

$$= \frac{1}{2}\left[\,3\log(4.5) - 3\log(2\alpha_F+3) - \left(\frac{3}{4} - \alpha_F\right) - \frac{1}{32}\left(\frac{81}{4} - (2\alpha_F+3)^2\right)\right]$$

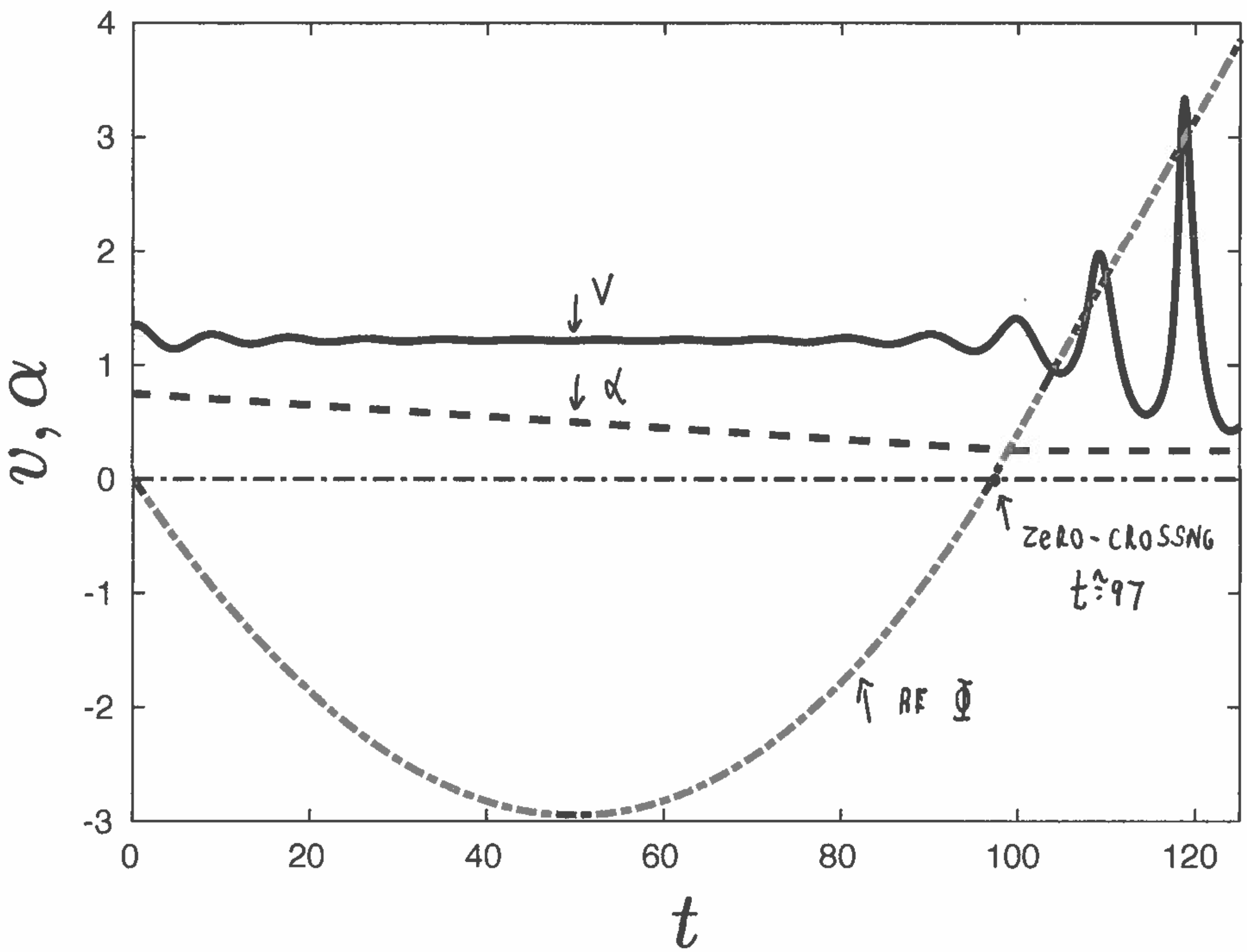
$$\mathrm{RE}\ \Phi = \frac{1}{2}\left[\,3\log\left(\frac{9}{2}\right) - 3\log(2\alpha_F+3) - \frac{3}{4} + \alpha_F - \frac{81}{128} + \frac{1}{32}(2\alpha_F+3)^2\right]$$

NOW SETTING $\mathrm{RE}\ \Phi = 0$ AND USING A ROOT-FINDER WE CALCULATE $\alpha_F \doteq .264$. THEREFORE, WE PREDICT THAT A HB WILL BE TRIGGERED WHEN

$$t_F = \frac{\alpha_i - \alpha_F}{\varepsilon} = \frac{.75 - .264}{.005} \simeq 97.$$

(Q6)

DELAYED HB FOR SELKOV MODEL (FULL NUMERICS)



IF $\alpha = \begin{cases} .75 - .005t \\ .25 & , t \geq 100 \end{cases}$ WE OBSERVE A DELAYED HB

THAT IS TRIGGERED NEAR WHERE $\text{RE}\,\Phi = \frac{1}{2}\int_0^{\tau}\left(\frac{6}{2\alpha+3} - 1 - \frac{1}{8}(2\alpha+3)\right)d\tau$

CROSSES THROUGH ZERO. THIS GAVE $\tau = .75 - .264$ OR $t \doteq 97$,

WITH $\varepsilon = .005$. OSCILLATION ARE OBSERVED NEAR THAT TIME.