Mathematical derivations of the paper "How does the inner retinal network shape the ganglion cells receptive field : a computational study"

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September 22, 2023

1 Mathematical derivations of the rest state properties.

We call "simple case" the situation described in section 2.1.4 of the paper: $W_B^A = -w^- \Gamma_B^A$, $W_A^B = w^+ \Gamma_A^B$ where $\Gamma_A^B = \Gamma_B^A$ are nearest neighbors adjacency matrices.

1.1 Characteristic times

From eq. (22) in the paper:

$$\tau_q = \frac{\tau_L}{1 + \frac{g_{CNO_T}}{g_L} + \sum_{Y,syn} \sum_{p \in Y} \frac{\lambda_q^{(Y,p)}}{g_L} \mathscr{N}^Y(V_p^*)}.$$

We assume $\mathscr{E}_{CNO_T}, \mathscr{E}_Y \neq 0$. We have:

$$\zeta_T = \frac{g_{CNO_T} \mathscr{E}_{CNO_T}}{C} \Rightarrow \frac{g_{CNO_T}}{g_L} = \tau_L \frac{\zeta_T}{\mathscr{E}_{CNO_T}};$$

$$W_q^{(Y,p)} = \frac{\lambda_q^{(Y,p)} \mathscr{E}_Y}{C} \Rightarrow \frac{\lambda_q^{(Y,p)}}{g_L} = \frac{\tau_L}{\mathscr{E}_Y} W_q^{(Y,p)}.$$

Thus:

$$\boxed{\tau_q = \frac{\tau_L}{1 + \tau_L \left(\frac{\zeta_T}{\mathscr{E}_{CNO_T}} + \sum_{Y,syn} \frac{1}{\mathscr{E}_Y} \sum_{p \in Y} W_q^{(Y,p)} \mathscr{N}^Y(V_p^*) \right)}}.$$

In the model, for a general connectivity matrix W_B^A, this gives:

$$\tau_{B_i} = \frac{\tau_L}{1 + \frac{\tau_L}{\mathscr{E}_A} \sum_{j=1}^N W_{B_i}^{A_j} \mathscr{N}^A(V_{A_j}^*)}.$$

In the simple case, if we neglect boundary effects, the connectivity is uniform in space, so that the rest state is spatially uniform. If the spatially uniform rest state of ACs, V_A^* is below threshold, then $\tau_{B_i} = \tau_L$. If it is above threshold:

$$\boxed{\tau_{B_i} \equiv \tau_B = \frac{\tau_L}{1 - \frac{2dw^- \tau_L}{\mathscr{E}_A}(V_A^* - \theta_A)}}. \tag{1}$$

where d is the lattice dimension. Likewise for ACs we have:

$$\tau_{A_j} = \frac{\tau_L}{1 + \tau_L \left(\frac{\zeta_A}{\mathscr{E}_{CNO_A}} + \frac{1}{\mathscr{E}_B} \sum_{i=1}^N W_{A_j}^{B_i} \mathscr{N}^B(V_{B_i}^*) \right)} \qquad \underset{\text{if} \quad V_B^* > \theta_B}{\overset{\Longrightarrow}{\text{simple case}}}$$

$$\boxed{\tau_{A_j} \equiv \tau_A = \frac{\tau_L}{1 + \tau_L \left(\frac{\zeta_A}{\mathscr{E}_{CNO_A}} + \frac{2dw^+}{\mathscr{E}_B}(V_B^* - \theta_B) \right)}}, \tag{2}$$

while $\tau_A = \frac{\tau_L}{1 + \tau_L \frac{\zeta_A}{\mathscr{E}_{CNO_A}}}$ if V_B^* is below threshold.

For RGCs we have:

$$\tau_{G_k} = \frac{\tau_L}{1 + \tau_L \left(\frac{\zeta_G}{\mathscr{E}_{CNO_G}} + \frac{1}{\mathscr{E}_B} \sum_{i=1}^N W_{G_k}^{B_i} \mathscr{N}^B(V_{B_i}^*) + \frac{1}{\mathscr{E}_A} \sum_{j=1}^N W_{G_k}^{A_j} \mathscr{N}^B(V_{A_j}^*) \right)}.$$

In the simple case, even if BCs and ACs rest voltages are uniform in space, RGCs may feel more the boundaries effect because of the Gaussian pooling which extends the connectivity on a quite wider range (of order $3\sigma_p$) than the nearest neighbours interactions of BCs ACs. We note $M_{G_k}^B = \sum_{i=1}^N W_{G_k}^{B_i}$ (resp. $M_{G_k}^A = \sum_{j=1}^N W_{G_k}^{A_j}$). We have, if $V_B^* > \theta_B, V_A^* > \theta_A$:

$$\boxed{\tau_{G_k} = \frac{\tau_L}{1 + \tau_L \left(\frac{\zeta_G}{\mathscr{E}_{CNO_G}} + \frac{M_{G_k}^B}{\mathscr{E}_B} \left(V_B^* - \theta_B \right) + \frac{M_{G_k}^A}{\mathscr{E}_A} \left(V_A^* - \theta_A \right) \right)}}. \tag{3}$$

In the paper, though, we will consider cells so far from the boundaries that $M_{G_k}^B$ and $M_{G_k}^A$ are independent of k.

The other configurations of voltages with respect to threshold can be easily computed.

1.2 Rest state

1.2.1 General case

The dynamics is given by:

$$\left\{\begin{array}{rcl} \frac{dV_{B_i}}{dt} & = & -\frac{1}{\tau_{B_i}} V_{B_i} + \sum_{j=1}^{N_A} W_{B_i}^{A_j} \mathcal{N}^{(A)}\left(V_{A_j}\right) + F_{B_i}(t), \quad i = 1\dots N \\ \frac{dV_{A_j}}{dt} & = & -\frac{1}{\tau_{A_j}} V_{A_j} + \sum_{i=1}^{N_B} W_{A_j}^{B_i} \mathcal{N}^{(B)}\left(V_{B_i}\right) + \zeta_A, \quad j = 1\dots N, \\ \frac{dV_{G_k}}{dt} & = & -\frac{1}{\tau_{G_k}} V_{G_k} + \sum_{i=1}^{N_B} W_{G_k}^{B_i} \mathcal{N}^{(B)}(V_{B_i}) + \sum_{j=1}^{N_A} W_{G_k}^{A_j} \mathcal{N}^{(A)}(V_{A_j}) + \zeta_G, \quad k = 1\dots N. \end{array}\right.$$

where $\tau_{B_i}, \tau_{A_j}, \tau_{G_k}$ are non linear functions of the rest state, as exposed in the previous section.

In the general case where characteristic times are not spatially uniform we introduce the diagonal $N \times N$ matrices of characteristic times $\mathcal{T}_B = \text{diag}\left[\tau_{B_i}\right]_{i=1\dots N}$, $\mathcal{T}_A = \text{diag}\left[\tau_{A_j}\right]_{j=1\dots N}$, $\mathcal{T}_G = \text{diag}\left[\tau_{G_k}\right]_{k=1\dots N}$. We use the slight abuse of notation $\mathcal{N}^{(A)}\left(\vec{V}_A\right)$ for the vector of entries $\mathcal{N}^{(A)}\left(V_{A_j}\right)$, $j = 1\dots N$, and write the dynamics in vector form:

$$\left\{\begin{array}{rcl} \frac{d\vec{V}_B}{dt} & = & -\mathcal{T}_B^{-1}.\vec{V}_B + W_B^A.\mathcal{N}^{(A)}\left(\vec{V}_A\right) + \vec{F}_B(t), \\ \frac{d\vec{V}_A}{dt} & = & -\mathcal{T}_A^{-1}.\vec{V}_A + W_A^B.\mathcal{N}^{(B)}\left(\vec{V}_B\right) + \zeta_A \vec{1}_N, \\ \frac{d\vec{V}_G}{dt} & = & -\mathcal{T}_G^{-1}.\vec{V}_G + W_G^B.\mathcal{N}^{(B)}(\vec{V}_B) + W_G^A.\mathcal{N}^{(A)}(\vec{V}_A) + \zeta_G \vec{1}_N. \end{array}\right.$$

where $\vec{1}_N$ is the unit vector in N dimension. The rest state vector is then given by:

$$\left\{\begin{array}{rcl} \vec{V}_B^* & = & \mathcal{T}_B.W_B^A.\mathcal{N}^{(A)}\left(\vec{V}_A^*\right); \\ \vec{V}_A^* & = & \mathcal{T}_A.\left[W_A^B.\mathcal{N}^{(B)}\left(\vec{V}_B^*\right) + \zeta_A \vec{1}_N\right]; \\ \vec{V}_G^* & = & \mathcal{T}_G.\left[W_G^B.\mathcal{N}^{(B)}\left(\vec{V}_B^*\right) + W_G^A.\mathcal{N}^{(A)}\left(\vec{V}_A^*\right) + \zeta_G \vec{1}_N\right]. \end{array}\right.$$

This leads to implicit piecewise linear equations of the form e.g. $\vec{V}_B^* = \mathcal{T}_B.W_B^A.\mathcal{N}^{(A)}\left(\mathcal{T}_A.\left[W_A^B.\mathcal{N}^{(B)}\left(\vec{V}_B^*\right) + \zeta_A \vec{1}_N\right]\right)$ which are not possible to solve in general especially because the characteristic time matrices do not commute with the connectivity matrices.

The situation is better in the case where characteristic times are spatially uniform. Assuming that rest states are above threshold gives:

$$\vec{V}_B^* = \tau_B W_B^A.\left(\tau_A W_A^B.\vec{V}_B^* - \tau_A \theta_B W_A^B.\vec{1}_N + \tau_A \zeta_A \vec{1}_N\right) - \tau_B \theta_A W_B^A.\vec{1}_N$$

$$\vec{V}_B^* = \tau_A \tau_B W_B^A.W_A^B.\vec{V}_B^* + \left(\tau_A \tau_B \zeta_A W_B^A - \tau_A \tau_B \theta_B W_B^A.W_A^B - \tau_B \theta_A W_B^A\right).\vec{1}_N$$

Assuming that $\mathscr{I}_N - \tau_A \tau_B W_B^A W_A^B$ is invertible, we obtain:

$$\boxed{\vec{V}_B^* = \tau_B \left(\mathscr{I}_N - \tau_A \tau_B W_B^A W_A^B \right)^{-1} . \left(\tau_A \zeta_A W_B^A - \tau_A \theta_B W_B^A W_A^B - \theta_A W_B^A \right) . \vec{1}_N}$$

Likewise, for $\vec{V}_A^*$:

$$\vec{V}_A^* = \tau_A W_A^B . \left(\tau_B W_B^A . \vec{V}_A^* - \tau_B \theta_A W_B^A . \vec{1}_N \right) - \tau_A \theta_B W_A^B . \vec{1}_N + \tau_A \zeta_A \vec{1}_N$$

$$\vec{V}_A^* = \tau_A \tau_B W_A^B . W_B^A . \vec{V}_A^* + \left(\tau_A \zeta_A - \tau_A \tau_B \theta_A W_A^B . W_B^A - \tau_A \theta_B W_A^B \right) . \vec{1}_N$$

Assuming that $\mathscr{I}_N - \tau_A \tau_B W_A^B . W_B^A$ is invertible, this gives:

$$\boxed{\vec{V}_A^* = \tau_A \left(\mathscr{I}_N - \tau_A \tau_B W_A^B . W_B^A \right)^{-1} . \left(\zeta_A - \tau_B \theta_A W_A^B . W_B^A - \theta_B W_A^B \right) . \vec{1}_N}$$

The voltage of RGCs is given by:

$$\boxed{\vec{V}_G^* = \tau_G \left[W_G^B . \mathscr{N}^{(B)} \left(\vec{V}_B^* \right) + W_G^A . \mathscr{N}^{(A)} \left(\vec{V}_A^* \right) + \zeta_G \vec{1}_N \right].}$$

1.2.2 Rest state in the simple case

Assuming that rest states are above threshold we have:

$$\begin{cases} V_B^* &= -2d\tau_B w^- V_A^* + 2d\tau_B w^- \theta_A \\ V_A^* &= 2d\tau_A w^+ V_B^* - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A \\ V_{G_k}^* &= \tau_G \left[M_{G_k}^B \left(V_B^* - \theta_B \right) + M_{G_k}^A \left(V_A^* - \theta_A \right) + \zeta_G \right] \end{cases}$$

In the following, we stick at the rest state of BCs and ACs, as the voltage of RGCs can be deduced from them. We have:

$$V_B^* = -2d\tau_B w^- \left(2d\tau_A w^+ V_B^* - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A \right) + 2d\tau_B w^- \theta_A$$

$$V_B^* = -4d^2 \tau_A \tau_B w^- w^+ V_B^* + 4d^2 \tau_A \tau_B w^- w^+ \theta_B - 2d\tau_B w^- \tau_A \zeta_A + 2d\tau_B w^- \theta_A$$

$$\boxed{V_B^* = \frac{4d^2 \tau_A \tau_B w^- w^+ \theta_B - 2d\tau_B w^- \tau_A \zeta_A + 2d\tau_B w^- \theta_A}{1 + 4d^2 \tau_A \tau_B w^- w^+}.} \tag{4}$$

$$V_A^* = 2d\tau_A w^+ \left(-2\tau_B w^- V_A^* + 2d\tau_B w^- \theta_A \right) - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A$$

$$V_A^* = -4d^2 \tau_A \tau_B w^- w^+ V_A^* + 4d^2 \tau_A \tau_B w^- w^+ \theta_A - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A$$

$$\boxed{V_A^* = \frac{4d^2 \tau_A \tau_B w^- w^+ \theta_A - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A}{1 + 4d^2 \tau_A \tau_B w^- w^+}.} \tag{5}$$

These results hold if both V_B^* and V_A^* are above threshold. If $V_B^* < \theta_B$, then $V_A^* = \tau_A \zeta_A$, $V_B^* = 2d\tau_B w^- \left(\theta_A - \tau_A \zeta_A \right)$. If $V_A^* < \theta_A$, $V_B^* = 0$, $V_A^* = \tau_A \left(\zeta_A - 2dw^+ \theta_B \right)$.

1.2.3 Conditions for the rest states to be above threshold. Dependence on CNO.

The rest state of BCs.

$$V_B^* = \frac{4d^2\tau_A\tau_B w^- w^+\theta_B - 2d\tau_B w^- \tau_A\,\zeta_A\, + 2d\tau_B w^- \theta_A}{1+4d^2\tau_A\tau_B w^- w^+} \geq \theta_B$$

$$\cancel{4d^2\tau_A\tau_B w^- w^+\theta_B} - 2d\tau_B w^- \tau_A\,\zeta_A\, + 2d\tau_B w^- \theta_A \geq \theta_B + \cancel{4d^2\tau_A\tau_B w^- w^+\theta_B}$$

$$-2d\tau_B w^- \tau_A\,\zeta_A \geq \theta_B - 2d\tau_B w^- \theta_A$$

$$\zeta_A \leq -\frac{\theta_B - 2d\tau_B w^- \theta_A}{2d\tau_B w^- \tau_A}.$$

Thus, the condition ensuring that the rest state of BCs is above threshold when applying CNO is:

$$\boxed{\zeta_A \leq -\frac{1}{\tau_A}\left(\frac{\theta_B}{2d\tau_B w^-} - \theta_A\right).} \tag{6}$$

Note that ζ_A can be positive or negative, depending on the modelling choice of the reversal potential $\mathscr{E}_{CNO_A}$. We shall stick at $\zeta_A > 0$.

The rest state of ACs.

$$V_A^* = \frac{4d^2\tau_A\tau_B w^- w^+\theta_A\, - 2d\tau_A w^+\theta_B\, + \tau_A\,\zeta_A}{1+4d^2\tau_A\tau_B w^- w^+} \geq \theta_A$$

$$\cancel{4d^2\tau_A\tau_B w^- w^+\theta_A}\, - 2d\tau_A w^+\theta_B\, + \tau_A\,\zeta_A \geq \theta_A + \cancel{4d^2\tau_A\tau_B w^- w^+\theta_A}$$

$$\boxed{\zeta_A \geq \frac{1}{\tau_A}\left(\theta_A + 2d\tau_A w^+\theta_B\right).} \tag{7}$$

Condition for the rest state of BCs and ACs to be above threshold.

$$\boxed{\frac{1}{\tau_A}\left(\theta_A + 2d\tau_A w^+\theta_B\right) \leq \zeta_A \leq -\frac{\theta_B - 2d\tau_B w^-\theta_A}{2d\tau_B w^- \tau_A}.} \tag{8}$$

This requires that:

$$2d\tau_B w^-\,\left(\theta_A + 2d\tau_A w^+\theta_B\right) \leq -\left(\theta_B - 2d\tau_B w^-\theta_A\right)$$

$$\cancel{2d\tau_B w^-\theta_A} + 4d^2\,\tau_A\,\tau_B\, w^+\, w^-\,\theta_B \leq -\theta_B + \cancel{2d\tau_B w^-\theta_A},$$

$$\left(1 + 4d^2\,\tau_A\,\tau_B\, w^+\, w^-\right)\,\theta_B \leq 0,$$

thus, $\theta_B \leq 0$.

In order for the rest states not be rectified in the absence of CNO it is necessary that $\theta_A + 2d\tau_A w^+\theta_B \leq 0$ thus $\theta_A \leq -2d\tau_A w^+\theta_B$. We may thus take $\theta_A = 0$, as we will do in the sequel. For excitatory CNO ($\zeta_A > 0$) the left hand side of (8) holds. Increasing ζ_A the rest state becomes rectified if $\zeta_A > -\frac{\theta_B - 2d\tau_B w^-\theta_A}{2d\tau_B w^-\tau_A} = -\frac{\theta_B}{2d\tau_B w^-\tau_A}$.

2 Variations with respect to CNO

The goal here is to compute the derivatives $\frac{\partial V_B^*}{\partial \zeta_A}, \frac{\partial V_A^*}{\partial \zeta_A}, \frac{\partial \tau_B}{\partial \zeta_A}, \frac{\partial \tau_A}{\partial \zeta_A}$ in order to see how these quantities evolve when increasing the CNO effect on ACs. The characteristic times of RGCs, τ_{G_k} are functions of BCs and ACs voltages and characteristic times so that we have essentially to solve the implicit equations linking $\tau_{B_i}, \tau_{A_j}, V_B^*, V_A^*$. In the simple case this implicit non linear system has the form:

$$\begin{cases} H_B(\tau_B, \tau_A, \zeta_A) & \equiv & \tau_B - \frac{\tau_L}{1+\frac{2d\tau_L}{\mathscr{E}_A}w^-\theta_A - \frac{2d\tau_L}{\mathscr{E}_A}w^- V_A^*(\tau_B,\tau_A)} = 0, \\ H_A(\tau_B, \tau_A, \zeta_A) & \equiv & \tau_A - \frac{\tau_L}{1-\frac{2d\tau_L}{\mathscr{E}_B}w^+\theta_B + \frac{\tau_L \zeta_A}{\mathscr{E}_{CNO_A}} + \frac{2d\tau_L}{\mathscr{E}_B}w^+ V_B^*(\tau_B,\tau_A)} = 0. \end{cases}, \tag{9}$$

The derivatives $\frac{d\tau_B}{\partial \zeta_A}, \frac{\partial \tau_A}{d\zeta_A}$ are given by the implicit function theorem $\begin{pmatrix} \frac{\partial \tau_B}{\partial \zeta_A} \\ \frac{\partial \tau_A}{\partial \zeta_A} \end{pmatrix} = -DH^{-1}.\vec{\nabla}_\zeta H$ assuming that DH, the Jacobian of $H = \begin{pmatrix} H_B \\ H_A \end{pmatrix}$, is invertible. This reads, in vector form:

$$\begin{pmatrix} \frac{d\tau_B}{d\zeta_A} \\ \frac{d\tau_A}{d\zeta_A} \end{pmatrix} = \frac{1}{\frac{\partial H_B}{\partial \tau_B}\frac{\partial H_A}{\partial \tau_A} - \frac{\partial H_B}{\partial \tau_A}\frac{\partial H_A}{\partial \tau_B}} \begin{pmatrix} -\frac{\partial H_A}{\partial \tau_A}\frac{\partial H_B}{\partial \zeta_A} & +\frac{\partial H_B}{\partial \tau_A}\frac{\partial H_A}{\partial \zeta_A} \\ \frac{\partial H_A}{\partial \tau_B}\frac{\partial H_B}{\partial \zeta_A} & -\frac{\partial H_B}{\partial \tau_B}\frac{\partial H_A}{\partial \zeta_A} \end{pmatrix}. \tag{10}$$

We therefore need to compute the partial derivatives of H.

2.1 Derivatives of H

$$\frac{\partial H_B}{\partial \tau_A} = -\frac{2d\tau_L}{\mathscr{E}_A}w^- \frac{\tau_L}{\left(1+\frac{2d\tau_L}{\mathscr{E}_A}w^-\theta_A - \frac{2d\tau_L}{\mathscr{E}_A}w^-V_A^*\right)^2}\frac{\partial V_A^*}{\partial \tau_A} = -\frac{2d}{\mathscr{E}_A}\tau_B^2 w^- \frac{\partial V_A^*}{\partial \tau_A}$$

$$\frac{\partial H_A}{\partial \tau_A} = 1 + \frac{2d\tau_L}{\mathscr{E}_B}w^+ \frac{\tau_L}{\left(1-\frac{2d\tau_L}{\mathscr{E}_B}w^+\theta_B + \frac{\tau_L\zeta_A}{\mathscr{E}_{CNO_A}} + \frac{2d\tau_L}{\mathscr{E}_B}w^+V_B^*(\tau_B,\tau_A)\right)^2}\frac{\partial V_B^*}{\partial \tau_A} = 1 + \frac{2d}{\mathscr{E}_B}w^+\tau_A^2\frac{\partial V_B^*}{\partial \tau_A}$$

$$\frac{\partial H_B}{\partial \tau_B} = 1 - \frac{2d\tau_L}{\mathscr{E}_A}w^- \frac{\tau_L}{\left(1+\frac{2d\tau_L}{\mathscr{E}_A}w^-\theta_A - \frac{2d\tau_L}{\mathscr{E}_A}w^-V_A^*\right)^2}\frac{\partial V_A^*}{\partial \tau_B} = 1 - \frac{2d}{\mathscr{E}_A}\tau_B^2 w^- \frac{\partial V_A^*}{\partial \tau_B}$$

$$\frac{\partial H_A}{\partial \tau_B} = \frac{2d\tau_L}{\mathscr{E}_B}w^+ \frac{\tau_L}{\left(1-\frac{2d\tau_L}{\mathscr{E}_B}w^+\theta_B + \frac{\tau_L\zeta_A}{\mathscr{E}_{CNO_A}} + \frac{2d\tau_L}{\mathscr{E}_B}w^+V_B^*(\tau_B,\tau_A)\right)^2}\frac{\partial V_B^*}{\partial \tau_B} = \frac{2d}{\mathscr{E}_B}w^+\tau_A^2\frac{\partial V_B^*}{\partial \tau_B}$$

$$\frac{\partial H_B}{\partial \zeta_A} = -\frac{2d\tau_L}{\mathscr{E}_A}w^- \frac{\tau_L}{\left(1+\frac{2d\tau_L}{\mathscr{E}_A}w^-\theta_A - \frac{2d\tau_L}{\mathscr{E}_A}w^-V_A^*\right)^2}\frac{\partial V_A^*}{\partial \zeta_A} = -\frac{2d}{\mathscr{E}_A}w^-\tau_B^2\frac{\partial V_A^*}{\partial \zeta_A}$$

$$\frac{\partial H_A}{\partial \zeta_A} = \frac{\tau_L}{\left(1-\frac{2d\tau_L}{\mathscr{E}_B}w^+\theta_B + \frac{\tau_L\zeta_A}{\mathscr{E}_{CNO_A}} + \frac{2d\tau_L}{\mathscr{E}_B}w^+V_B^*\right)^2}\left(\frac{\tau_L}{\mathscr{E}_{CNO_A}} + \frac{2dw^+\tau_L}{\mathscr{E}_B}\frac{\partial V_B^*}{\partial \zeta_A}\right) = \tau_A^2\left(\frac{1}{\mathscr{E}_{CNO_A}} + \frac{2dw^+}{\mathscr{E}_B}\frac{\partial V_B^*}{\partial \zeta_A}\right)$$

2.2 Derivatives of voltages

2.2.1 Derivatives of voltages with respect to characteristic times

$$\frac{\partial V_A^*}{\partial \tau_B} = \frac{\partial}{\partial \tau_B}\left(\frac{4d^2\tau_A\tau_B w^- w^+\theta_A - 2d\tau_A w^+\theta_B + \tau_A\zeta_A}{1+4d^2\tau_A\tau_B w^- w^+}\right)$$

$$= \frac{4d^2\tau_A w^- w^+\theta_A\left(1+4d^2\tau_A\tau_B w^- w^+\right) - 4d^2\tau_A w^- w^+\left(4d^2\tau_A\tau_B w^- w^+\theta_A - 2d\tau_A w^+\theta_B + \tau_A\zeta_A\right)}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$= \frac{4d^2\tau_A w^- w^+\theta_A + \cancel{16d^4\tau_A^2\tau_B {w^-}^2 {w^+}^2\theta_A} - \cancel{16d^4\tau_A^2\tau_B {w^-}^2 {w^+}^2\theta_A} + 8d^3\tau_A^2 w^- {w^+}^2\theta_B - 4d^2\tau_A^2 w^- w^+\zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$= \frac{4d^2\tau_A w^- w^+\theta_A + 8d^3\tau_A^2 w^- {w^+}^2\theta_B - 4d^2\tau_A^2 w^- w^+\zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$\boxed{\frac{\partial V_A^*}{\partial \tau_B} = 4d^2\tau_A w^- w^+\,\frac{\theta_A + 2d\tau_A w^+\theta_B - \tau_A\zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} = 4d^2\tau_A w^- w^+\,\frac{2d\tau_A w^+\theta_B - \tau_A\zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} < 0,} \tag{11}$$

where the last equality and inequality hold because we set $\theta_A = 0$, $\theta_B < 0$, $\zeta_A > 0$.

$$\frac{\partial V_A^*}{\partial \tau_A} = \frac{\partial}{\partial \tau_A}\left(\frac{2d\tau_A w^+\left[2d\tau_B w^-\theta_A - \theta_B\right] + \tau_A\zeta_A}{1+4d^2\tau_A\tau_B w^- w^+}\right) = \frac{\partial}{\partial \tau_A}\left(\frac{4d^2\tau_A\tau_B w^- w^+\theta_A - 2d\tau_A w^+\theta_B + \tau_A\zeta_A}{1+4d^2\tau_A\tau_B w^- w^+}\right)$$

$$= \frac{\begin{bmatrix} \left(4d^2 w^- w^+\tau_B\theta_A - 2dw^+\theta_B + \zeta_A\right)\left(1+4d^2\tau_A\tau_B w^- w^+\right) \\ -4d^2\tau_B w^- w^+\left(4d^2\tau_A\tau_B w^- w^+\theta_A - 2d\tau_A w^+\theta_B + \tau_A\zeta_A\right) \end{bmatrix}}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$= \frac{\begin{bmatrix} 4d^2 w^- w^+\tau_B\theta_A - 2dw^+\theta_B + \zeta_A \\ +\cancel{16d^4\tau_A\tau_B^2 {w^-}^2 {w^+}^2\theta_A} - \cancel{8d^3\tau_A\tau_B w^- {w^+}^2\theta_B} + \cancel{4d^2\tau_A\tau_B w^- w^+\zeta_A} \\ -\cancel{16d^4\tau_A\tau_B^2 {w^-}^2 {w^+}^2\theta_A} + \cancel{8d^3\tau_A\tau_B w^- {w^+}^2\theta_B} - \cancel{4d^2\tau_A\tau_B w^- w^+\zeta_A} \end{bmatrix}}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$\boxed{\frac{\partial V_A^*}{\partial \tau_A} = \frac{4d^2 w^- w^+\tau_B\theta_A - 2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} = \frac{-2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} > 0.} \tag{12}$$

$$\frac{\partial V_B^*}{\partial \tau_B} = \frac{\partial}{\partial \tau_B}\left(\frac{2d\tau_B w^-\left[2d\tau_A w^+\theta_B - \tau_A\zeta_A + \theta_A\right]}{1+4d^2\tau_A\tau_B w^- w^+}\right)$$

$$= \frac{\begin{bmatrix} 2dw^-\left(2d\tau_A w^+\theta_B - \tau_A\zeta_A + \theta_A\right)\left(1+4d^2\tau_A\tau_B w^- w^+\right) \\ -4d^2\tau_A w^- w^+\left(4d^2\tau_A\tau_B w^- w^+\theta_B - 2d\tau_B w^-\tau_A\zeta_A + 2d\tau_B w^-\theta_A\right) \end{bmatrix}}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$$

$$
= \frac{\left[\begin{array}{l} 2dw^- \Big(2d\tau_A w^+ \theta_B - \tau_A \zeta_A + \theta_A + 8d^3 \tau_A^2 \tau_B w^- {w^+}^2 \theta_B - 4d^2 \tau_A^2 \tau_B w^- w^+ \zeta_A + 4d^2 \tau_A \tau_B w^- w^+ \theta_A \Big) \\ -16d^4 \tau_A^2 \tau_B {w^-}^2 {w^+}^2 \theta_B + 8d^3 \tau_A^2 \tau_B {w^-}^2 w^+ \zeta_A - 8d^3 \tau_A \tau_B {w^-}^2 w^+ \theta_A \end{array}\right]}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2}
$$

$$
= \frac{\left[\begin{array}{l} 4d^2 \tau_A w^- w^+ \theta_B - 2d\tau_A w^- \zeta_A + 2dw^- \theta_A + \cancel{16d^4 \tau_A^2 \tau_B {w^-}^2 {w^+}^2} \theta_B - \cancel{8d^3 \tau_A^2 \tau_B {w^-}^2 w^+ \zeta_A} + \cancel{8d^3 \tau_A \tau_B {w^-}^2 w^+ \theta_A} \\ \cancel{-16d^4 \tau_A^2 \tau_B {w^-}^2 {w^+}^2} \theta_B + \cancel{8d^3 \tau_A^2 \tau_B {w^-}^2 w^+ \zeta_A} - \cancel{8d^3 \tau_A \tau_B {w^-}^2 w^+ \theta_A} \end{array}\right]}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2}
$$

$$
\boxed{\frac{\partial V_B^*}{\partial \tau_B} = 2dw^- \frac{2d\tau_A w^+ \theta_B - \tau_A \zeta_A + \theta_A}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2} = 2dw^- \frac{2d\tau_A w^+ \theta_B - \tau_A \zeta_A}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2} < 0.} \tag{13}
$$

$$
\frac{\partial V_B^*}{\partial \tau_A} = \frac{\partial}{\partial \tau_A} \left(\frac{2d\tau_B w^- \left[2d\tau_A w^+ \theta_B - \tau_A \zeta_A + \theta_A\right]}{1 + 4d^2 \tau_A \tau_B w^- w^+} \right)
$$

$$
= \frac{\left[\begin{array}{l} \left(4d^2 \tau_B w^- w^+ \theta_B - 2d\tau_B w^- \zeta_A\right)\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right) \\ -4d^2 \tau_B w^- w^+ \left(4d^2 \tau_A \tau_B w^- w^+ \theta_B - 2d\tau_A \tau_B w^- \zeta_A + 2d\tau_B w^- \theta_A\right) \end{array}\right]}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2}
$$

$$
= \frac{\left[\begin{array}{l} 4d^2 \tau_B w^- w^+ \theta_B - 2d\tau_B w^- \zeta_A \\ \cancel{+16d^4 \tau_A \tau_B^2 {w^-}^2 {w^+}^2} \theta_B - \cancel{8d^3 \tau_A \tau_B^2 {w^-}^2 w^+ \zeta_A} \\ \cancel{-16d^4 \tau_A \tau_B^2 {w^-}^2 {w^+}^2} \theta_B + \cancel{8d^3 \tau_A \tau_B^2 {w^-}^2 w^+ \zeta_A} - 8d^3 \tau_B^2 {w^-}^2 w^+ \theta_A \end{array}\right]}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2}
$$

$$
\boxed{\frac{\partial V_B^*}{\partial \tau_A} = 2d\tau_B w^- \frac{2dw^+ \theta_B - \zeta_A - 4d^2 \tau_B w^- w^+ \theta_A}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2} = 2d\tau_B w^- \frac{2dw^+ \theta_B - \zeta_A}{\left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2} < 0.} \tag{14}
$$

Note that in the general situation where $\theta_B, \theta_A, \zeta_A$ have any sign these derivatives can be behave in quite different way, depending on the parameters domain.

2.2.2 Derivatives of voltages with respect to ζ_A

$$
\frac{\partial V_B^*}{\partial \zeta_A} = \frac{\partial}{\partial \zeta_A} \left(\frac{2d\tau_B w^- \left[2d\tau_A w^+ \theta_B - \tau_A \zeta_A + \theta_A\right]}{1 + 4d^2 \tau_A \tau_B w^- w^+} \right) = -\frac{2d\tau_A \tau_B w^-}{1 + 4d^2 \tau_A \tau_B w^- w^+} \left(= -2d\tau_B w^- \frac{\partial V_A^*}{\partial \zeta_A} \right)
$$

$$
\boxed{\frac{\partial V_B^*}{\partial \zeta_A} = -\frac{2d\tau_A \tau_B w^-}{1 + 4d^2 \tau_A \tau_B w^- w^+} \leq 0} \tag{15}
$$

$$
\frac{\partial V_A^*}{\partial \zeta_A} = \frac{\partial}{\partial \zeta_A} \left(\frac{4d^2 \tau_A \tau_B w^- w^+ \theta_A - 2d\tau_A w^+ \theta_B + \tau_A \zeta_A}{1 + 4d^2 \tau_A \tau_B w^- w^+} \right) = \frac{\tau_A}{1 + 4d^2 \tau_A \tau_B w^- w^+}
$$

$$
\boxed{\frac{\partial V_A^*}{\partial \zeta_A} = \frac{\tau_A}{1 + 4d^2 \tau_A \tau_B w^- w^+} \geq 0} \tag{16}
$$

This result is quite expected. BCs get more hyperpolarized when the excitatory effect of CNO on ACs increases, while ACs get more depolarized when ζ_A increases.

2.2.3 Determinant of DH

$$\det H = \frac{\partial H_B}{\partial \tau_B}\frac{\partial H_A}{\partial \tau_A} - \frac{\partial H_B}{\partial \tau_A}\frac{\partial H_A}{\partial \tau_B}$$

$$= \left(\left(1 - \frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \tau_B} \right) \left(1 + \frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \frac{\partial V_B^*}{\partial \tau_A} \right) \right) + \left(\frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \tau_A} \right) \left(\frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \frac{\partial V_B^*}{\partial \tau_B} \right)$$

$$= 1 - \frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \tau_B} + \frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \frac{\partial V_B^*}{\partial \tau_A} - \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \frac{\partial V_A^*}{\partial \tau_B}\frac{\partial V_B^*}{\partial \tau_A} + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \frac{\partial V_A^*}{\partial \tau_A}\frac{\partial V_B^*}{\partial \tau_B}$$

$$= \left(\begin{array}{l} 1 - \frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \underbrace{\frac{\partial V_A^*}{\partial \tau_B}}_{2d\tau_A w^+ \frac{\partial V_B^*}{\partial \tau_B}} + \frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \underbrace{\frac{\partial V_B^*}{\partial \tau_A}}_{-2d\tau_B w^- \frac{\partial V_A^*}{\partial \tau_A}} \\ + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \underbrace{\left(\frac{\partial V_A^*}{\partial \tau_A}\frac{\partial V_B^*}{\partial \tau_B} - \underbrace{\frac{\partial V_A^*}{\partial \tau_B}}_{2d\tau_A w^+ \frac{\partial V_B^*}{\partial \tau_B}} \underbrace{\frac{\partial V_B^*}{\partial \tau_A}}_{-2d\tau_B w^- \frac{\partial V_A^*}{\partial \tau_A}} \right)}_{\left(1+4d^2\tau_A\tau_B w^- w^+\right)\frac{\partial V_A^*}{\partial \tau_A}\frac{\partial V_B^*}{\partial \tau_B}} \end{array} \right)$$

$$= \left(\begin{array}{l} 1 - \frac{4d^2 \tau_A \tau_B^2 w^- w^+}{\mathscr{E}_A} \frac{\partial V_B^*}{\partial \tau_B} - \frac{4d^2 \tau_B \tau_A^2 w^- w^+}{\mathscr{E}_B} \frac{\partial V_A^*}{\partial \tau_A} \\ + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right) \frac{\partial V_A^*}{\partial \tau_A}\frac{\partial V_B^*}{\partial \tau_B} \end{array} \right)$$

$$= \left(1 - \frac{4d^2 \tau_A \tau_B^2 w^- w^+}{\mathscr{E}_A} \underbrace{\frac{\partial V_B^*}{\partial \tau_B}}_{2dw^- \frac{\theta_A + 2d\tau_A w^+ \theta_B - \tau_A \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}} \right) \left(1 - \frac{4d^2 \tau_B \tau_A^2 w^- w^+}{\mathscr{E}_B} \underbrace{\frac{\partial V_A^*}{\partial \tau_A}}_{\frac{4d^2\tau_B w^- w^+ \theta_A - 2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}} \right) + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \underbrace{\frac{\partial V_A^*}{\partial \tau_A}}_{\frac{4d^2\tau_B w^- w^+ \theta_A - 2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}} \underbrace{\frac{\partial V_B^*}{\partial \tau_B}}_{2dw^- \frac{\theta_A + 2d\tau_A w^+ \theta_B - \tau_A \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}}$$

We assume $\theta_A = 0$, $\theta_B \leq 0$, $\zeta_A \geq 0$

$$\det H = \left(1 - \frac{4d^2 \tau_A \tau_B^2 w^- w^+}{\mathscr{E}_A} \left(2dw^- \frac{2d\tau_A w^+ \theta_B - \tau_A \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right) \right) \left(1 - \frac{4d^2 \tau_B \tau_A^2 w^- w^+}{\mathscr{E}_B} \left(\frac{-2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right) \right) + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} \tau_A^2 \tau_B^2 w^- w^+ \left(\frac{-2dw^+\theta_B + \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right) \left(2dw^- \frac{2d\tau_A w^+ \theta_B - \tau_A \zeta_A}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right)$$

$$= \left(1 + \frac{8d^3 \tau_A^2 \tau_B^2 w^{-2} w^+}{\mathscr{E}_A} \frac{\zeta_A - 2dw^+\theta_B}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right) \left(1 - \frac{4d^2 \tau_B \tau_A^2 w^- w^+}{\mathscr{E}_B} \frac{\zeta_A - 2dw^+\theta_B}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2} \right) - \frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} \tau_A^3 \tau_B^2 w^{-2} w^+ \frac{\left(\zeta_A - 2dw^+\theta_B\right)^2}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^4}$$

Setting $u = \frac{\zeta_A - 2dw^+\theta_B}{\left(1+4d^2\tau_A\tau_B w^- w^+\right)^2}$ gives:

$$\det H = \left(1 + \frac{8d^3 \tau_A^2 \tau_B^2 w^{-2} w^+}{\mathscr{E}_A} u \right) \left(1 - \frac{4d^2 \tau_B \tau_A^2 w^- w^+}{\mathscr{E}_B} u \right) - \frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} \tau_A^3 \tau_B^2 w^{-2} w^+ u^2$$

$$= \underbrace{1}_{c} + \underbrace{4d^2 \tau_B \tau_A^2 w^- w^+ \left(\frac{2dw^- \tau_B}{\mathscr{E}_A} - \frac{1}{\mathscr{E}_B} \right) u}_{b} \underbrace{- \frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} \tau_A^3 \tau_B^2 w^{-2} w^+ \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right) u^2}_{a}$$

This second order polynomial has two roots:

$$u_1, u_2 = -\frac{b}{2a} \pm \frac{\sqrt{\Delta}}{2a},$$

where:

$$\Delta = 16d^4 \tau_B^2 \tau_A^4 {w^-}^{-2} {w^+}^2 \left(\frac{2dw^- \tau_B}{\mathscr{E}_A} - \frac{1}{\mathscr{E}_B} \right)^2 + \frac{32d^3}{\mathscr{E}_A \mathscr{E}_B} \tau_A^3 \tau_B^2 {w^-}^{-2} w^+ \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right).$$

This quantity is positive if:

$$\cancel{16d^4} \textcircled{d} \cancel{\tau_B^2} \tau_A^{\cancel{4}\textcircled{1}} \cancel{{w^-}^{-2}} {w^+}^{\cancel{2}\textcircled{1}} \left(\frac{2dw^- \tau_B}{\mathscr{E}_A} - \frac{1}{\mathscr{E}_B} \right)^2 > -\frac{\cancel{32d^3}\textcircled{2}}{\mathscr{E}_A \mathscr{E}_B} \cancel{\tau_A^3} \cancel{\tau_B^2} \cancel{{w^-}^{-2}} \cancel{w^+} \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right)$$

$$\frac{4d^3 \tau_A \tau_B^2 w^{-2} w^+}{\mathscr{E}_A^2} - \frac{4d^2 \tau_A \tau_B w^- w^+}{\mathscr{E}_A \mathscr{E}_B} + \frac{d \tau_A w^+}{\mathscr{E}_B^2} > -\frac{2}{\mathscr{E}_A \mathscr{E}_B} - \frac{8d^2 \tau_A \tau_B w^- w^+}{\mathscr{E}_A \mathscr{E}_B}$$

$$\frac{4d^3 \tau_A \tau_B^2 w^{-2} w^+}{\mathscr{E}_A^2} + \frac{4d^2 \tau_A \tau_B w^- w^+}{\mathscr{E}_A \mathscr{E}_B} + \frac{2}{\mathscr{E}_A \mathscr{E}_B} + \frac{d \tau_A w^+}{\mathscr{E}_B^2} > 0$$

$$d \tau_A w^+ \left(\frac{4d^2 \tau_B^2 w^{-2}}{\mathscr{E}_A^2} + \frac{4d \tau_B w^-}{\mathscr{E}_A \mathscr{E}_B} + \frac{1}{\mathscr{E}_B^2} \right) > -\frac{2}{\mathscr{E}_A \mathscr{E}_B}$$

$$\boxed{\left(\frac{2d \tau_B w^-}{\mathscr{E}_A} + \frac{1}{\mathscr{E}_B} \right)^2 > -\frac{2}{\mathscr{E}_A \mathscr{E}_B} \frac{1}{d \tau_A w^+}.} \tag{17}$$

Note that the rhs is positive because $\mathscr{E}_A < 0, \mathscr{E}_B > 0$. For the same reason,

$$a = -\frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} \tau_A^3 \tau_B^2 {w^-}^{-2} w^+ \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right) > 0.$$

Thus, if (17) does not hold, there is no real solution to $\det H = 0$ and $\det H > 0$. If (17) holds u_1, u_2 are real and $\det H < 0$ if $u_1 < u < u_2$.

This gives conditions on ζ_A using the relation $\zeta_A = \left(1 + 4d^2 \tau_A \tau_B w^- w^+ \right)^2 u + 2dw^+ \theta_B$.

2.2.4 Numerator of $\frac{\partial \tau_B}{\partial \zeta_A}$

$$-\frac{\partial H_A}{\partial \tau_A} \frac{\partial H_B}{\partial \zeta_A} + \frac{\partial H_B}{\partial \tau_A} \frac{\partial H_A}{\partial \zeta_A} =$$

$$\left(1 + \frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \frac{\partial V_B^*}{\partial \tau_A} \right) \frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \zeta_A} - \frac{2d}{\mathscr{E}_A} w^- \tau_A^2 \tau_B^2 \frac{\partial V_A^*}{\partial \tau_A} \left(\frac{1}{\mathscr{E}_{CNO_A}} + \frac{2dw^+}{\mathscr{E}_B} \frac{\partial V_B^*}{\partial \zeta_A} \right) =$$

$$\frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \zeta_A} + \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} w^- w^+ \tau_A^2 \tau_B^2 \underbrace{\frac{\partial V_B^*}{\partial \tau_A}}_{-2d \tau_B w^- \frac{\partial V_A^*}{\partial \tau_A}} \frac{\partial V_A^*}{\partial \zeta_A} - \frac{2d}{\mathscr{E}_A \mathscr{E}_{CNO_A}} w^- \tau_A^2 \tau_B^2 \frac{\partial V_A^*}{\partial \tau_A} - \frac{4d^2}{\mathscr{E}_A \mathscr{E}_B} w^- w^+ \tau_A^2 \tau_B^2 \frac{\partial V_A^*}{\partial \tau_A} \underbrace{\frac{\partial V_B^*}{\partial \zeta_A}}_{-2d \tau_B w^- \frac{\partial V_A^*}{\partial \zeta_A}}$$

$$= \frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \zeta_A} - \cancel{\frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} w^{-2} w^+ \tau_A^2 \tau_B^3 \frac{\partial V_A^*}{\partial \tau_A} \frac{\partial V_A^*}{\partial \zeta_A}} - \frac{2d}{\mathscr{E}_A \mathscr{E}_{CNO_A}} w^- \tau_A^2 \tau_B^2 \frac{\partial V_A^*}{\partial \tau_A} + \cancel{\frac{8d^3}{\mathscr{E}_A \mathscr{E}_B} w^{-2} w^+ \tau_A^2 \tau_B^3 \frac{\partial V_A^*}{\partial \tau_A} \frac{\partial V_A^*}{\partial \zeta_A}}$$

$$= \underbrace{\frac{2d}{\mathscr{E}_A} w^- \tau_B^2}_{<0} \left(\frac{\partial V_A^*}{\partial \zeta_A} - \frac{1}{\mathscr{E}_{CNO_A}} \tau_A^2 \frac{\partial V_A^*}{\partial \tau_A} \right)$$

We have:

$$\underbrace{\frac{\partial V_A^*}{\partial \zeta_A}}_{\frac{\tau_A}{1+4d^2 \tau_A \tau_B w^- w^+}} - \frac{1}{\mathscr{E}_{CNO_A}} \tau_A^2 \underbrace{\frac{\partial V_A^*}{\partial \tau_A}}_{\frac{4d^2 \tau_B w^- w^+ \theta_A - 2dw^+ \theta_B + \zeta_A}{\left(1+4d^2 \tau_A \tau_B w^- w^+\right)^2}} \overset{\theta_A=0}{=}$$

$$\frac{\tau_A \mathscr{E}_{CNO_A} \left(1 + 4d^2 \tau_A \tau_B w^- w^+\right) - \tau_A^2 \left(\zeta_A - 2dw^+ \theta_B\right)}{\underbrace{\mathscr{E}_{CNO_A}}_{>0} \left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2}$$

This term is positive if:

$$\mathscr{E}_{CNO_A} \left(\frac{1}{\tau_A} + 4d^2 \tau_B w^- w^+ \right) + 2dw^+ \theta_B \geq \zeta_A$$

Thus the numerator

$$-\frac{\partial H_A}{\partial \tau_A} \frac{\partial H_B}{\partial \zeta_A} + \frac{\partial H_B}{\partial \tau_A} \frac{\partial H_A}{\partial \zeta_A}$$

is positive if:

$$\boxed{\zeta_A \geq \mathscr{E}_{CNO_A} \left(\frac{1}{\tau_A} + 4d^2 \tau_B w^- w^+ \right) + 2dw^+ \theta_B.} \tag{18}$$

(Recall that $\frac{2d}{\mathscr{E}_A} w^- \tau_B^2 < 0$).

Combining this condition with the conditions on the sign of $\det H$ shows that the sign of $\frac{\partial \tau_B}{\partial \zeta_A}$ depends of the models parameters. For example, it is positive in the domain:

$$\boxed{\left\{ \left(\frac{2d\tau_B w^-}{\mathscr{E}_A} + \frac{1}{\mathscr{E}_B} \right)^2 > -\frac{2}{\mathscr{E}_A \mathscr{E}_B} \frac{1}{d\tau_A w^+} \right\} \cap \left\{ \zeta_A > \mathscr{E}_{CNO_A} \left(\frac{1}{\tau_A} + 4d^2 \tau_B w^- w^+ \right) + 2dw^+ \theta_B \right\},} \tag{19}$$

and negative in the domain:

$$\boxed{\left\{ \left(\frac{2d\tau_B w^-}{\mathscr{E}_A} + \frac{1}{\mathscr{E}_B} \right)^2 > -\frac{2}{\mathscr{E}_A \mathscr{E}_B} \frac{1}{d\tau_A w^+} \right\} \cap \left\{ \zeta_A < \mathscr{E}_{CNO_A} \left(\frac{1}{\tau_A} + 4d^2 \tau_B w^- w^+ \right) + 2dw^+ \theta_B \right\}.} \tag{20}$$

2.2.5 Numerator of $\frac{\partial \tau_A}{\partial \zeta_A}$

$$\frac{\partial H_A}{\partial \tau_B}\frac{\partial H_B}{\partial \zeta_A} - \frac{\partial H_B}{\partial \tau_B}\frac{\partial H_A}{\partial \zeta_A} = -\frac{2d}{\mathscr{E}_B} w^+ \tau_A^2 \frac{\partial V_B^*}{\partial \tau_B}.\frac{2d}{\mathscr{E}_A} w^- \tau_B^2 \frac{\partial V_A^*}{\partial \zeta_A} - \left(1-\frac{2d}{\mathscr{E}_A}w^-\tau_B^2\frac{\partial V_A^*}{\partial \tau_B}\right)\tau_A^2\left(\frac{1}{\mathscr{E}_{CNO_A}}+\frac{2dw^+}{\mathscr{E}_B}\frac{\partial V_B^*}{\partial\zeta_A}\right)$$

$$= -\frac{4d^2}{\mathscr{E}_B\mathscr{E}_A}\tau_A^2\tau_B^2 w^- w^+ \frac{\partial V_B^*}{\partial\tau_B}\frac{\partial V_A^*}{\partial\zeta_A} - \frac{\tau_A^2}{\mathscr{E}_{CNO_A}} + \frac{2d}{\mathscr{E}_A\mathscr{E}_{CNO_A}}\tau_A^2\tau_B^2 w^-\frac{\partial V_A^*}{\partial\tau_B} - \frac{2d\tau_A^2 w^+}{\mathscr{E}_B}\frac{\partial V_B^*}{\partial \zeta_A} + \frac{4d^2}{\mathscr{E}_B\mathscr{E}_A}\tau_A^2\tau_B^2 w^- w^+ \frac{\partial V_A^*}{\partial\tau_B}\frac{\partial V_B^*}{\partial\zeta_A}$$

$$= \tau_A^2 \left(\begin{array}{c} -\frac{1}{\mathscr{E}_{CNO_A}} + \frac{2d}{\mathscr{E}_A\mathscr{E}_{CNO_A}}\tau_B^2 w^- \times \underbrace{\frac{\partial V_A^*}{\partial \tau_B}}_{\underbrace{4d^2\tau_A w^- w^+ \frac{\cancel{\theta_A} + 2d\tau_A w^+\theta_B - \tau_A\zeta_A}{(1+4d^2\tau_A\tau_B w^- w^+)^2}}_{-4d^2\tau_A^2 w^- w^+ u}} - \frac{2dw^+}{\mathscr{E}_B} \times \underbrace{\frac{\partial V_B^*}{\partial \zeta_A}}_{-\frac{2d\tau_A\tau_B w^-}{1+4d^2\tau_A\tau_B w^- w^+}} \\ + \frac{4d^2}{\mathscr{E}_B\mathscr{E}_A}\tau_B^2 w^- w^+ \left(\begin{array}{c} \underbrace{\frac{\partial V_A^*}{\partial \tau_B}}_{\underbrace{4d^2\tau_A w^- w^+ \frac{\cancel{\theta_A} + 2d\tau_A w^+\theta_B - \tau_A\zeta_A}{(1+4d^2\tau_A\tau_B w^- w^+)^2}}_{-4d^2\tau_A^2 w^- w^+ u}} \times \underbrace{\frac{\partial V_B^*}{\partial \zeta_A}}_{-\frac{2d\tau_A\tau_B w^-}{1+4d^2\tau_A\tau_B w^- w^+}} \\ - \underbrace{\frac{\partial V_B^*}{\partial \tau_B}}_{\underbrace{2dw^- \frac{\cancel{\theta_A} + 2d\tau_A w^+\theta_B - \tau_A\zeta_A}{(1+4d^2\tau_A\tau_B w^- w^+)^2}}_{-2dw^-\tau_A u}} \times \underbrace{\frac{\partial V_A^*}{\partial \zeta_A}}_{\frac{\tau_A}{1+4d^2\tau_A\tau_B w^- w^+}} \end{array} \right) \end{array} \right)$$

$$= \tau_A^2 \left(-\frac{1}{\mathscr{E}_{CNO_A}} - \frac{8d^3\tau_A^2\tau_B^2 {w^-}^2 w^+}{\mathscr{E}_A\mathscr{E}_{CNO_A}} u + \frac{1}{\mathscr{E}_B}\frac{4d^2\tau_A\tau_B w^- w^+}{1+4d^2\tau_A\tau_B w^- w^+} + \underbrace{\frac{1}{\mathscr{E}_B\mathscr{E}_A}\frac{32d^5\tau_B^3\tau_A^3 {w^-}^3 {w^+}^2}{1+4d^2\tau_A\tau_B w^- w^+} u + \frac{1}{\mathscr{E}_B\mathscr{E}_A}\frac{8d^3\tau_B^2\tau_A^2 {w^-}^2 w^+}{1+4d^2\tau_A\tau_B w^- w^+} u}_{\frac{8d^3\tau_B^2\tau_A^2 {w^-}^2 w^+}{\mathscr{E}_B\mathscr{E}_A}} \right).$$

The numerator is positive if:

$$-\frac{1}{\mathscr{E}_{CNO_A}} + \frac{1}{\mathscr{E}_B}\frac{4d^2\tau_A\tau_B w^- w^+}{1+4d^2\tau_A\tau_B w^- w^+} + \frac{8d^3\tau_A^2\tau_B^2 {w^-}^2 w^+}{\mathscr{E}_A}\left[\frac{1}{\mathscr{E}_B} - \frac{1}{\mathscr{E}_{CNO_A}}\right] u > 0$$

The sign of $\left[\frac{1}{\mathscr{E}_B} - \frac{1}{\mathscr{E}_{CNO_A}}\right]$ can be anything. Assuming it is positive ($\mathscr{E}_B < \mathscr{E}_{CNO_A}$):

$$u > \equiv u_{NA} = -\mathscr{E}_A \frac{\frac{4d^2\tau_A\tau_B w^- w^+}{\mathscr{E}_B(1+4d^2\tau_A\tau_B w^- w^+)} - \frac{1}{\mathscr{E}_{CNO_A}}}{8d^3\tau_A^2\tau_B^2 {w^-}^2 w^+ \left(\frac{1}{\mathscr{E}_B} - \frac{1}{\mathscr{E}_{CNO_A}}\right)},$$

so that $\frac{\partial H_A}{\partial \tau_B} \frac{\partial H_B}{\partial \zeta_A} - \frac{\partial H_B}{\partial \tau_B} \frac{\partial H_A}{\partial \zeta_A} > 0$ if :

$$\boxed{\zeta_A > \zeta_{NA} = 2dw^+ \theta_B + \left(1 + 4d^2 \tau_A \tau_B w^- w^+\right)^2 u_{NA}.} \tag{21}$$

Combined with the conditions fixing the sign of $\det H$ this provides domains where the sign of $\frac{\partial \tau_A}{\partial \zeta_A}$ is fixed, positive or negative, similarly to (19) or (20).