

A Extraction of oscillation amplitude from the autocorrelogram

When estimating the parameters of the model corresponding to Parkinson's disease, we require the model to produce oscillations with the same amplitude as observed in monkey models of the syndrome. However the average minimum and maximum firing rates within an oscillatory cycle are not typically reported in the literature, instead including autocorrelograms of the firing rate. In this appendix we describe how to extract information on the amplitude of oscillations from the autocorrelogram.

This method is based on the assumption that an oscillatory firing rate $s(t)$ can be considered as a sinusoidal signal with accumulative noise in the phase. This may be expressed using the equation:

$$s(t) = A \sin(t + \phi(t)) + B \quad (1)$$

where A is the amplitude of the oscillation, B the mean firing rate and $\phi(t)$ a Wiener process (which is the integration of a random signal). The Wiener process can be modelled as:

$$\frac{d\phi}{dt} = \mathcal{N}(0, dt \cdot \sigma^2) \quad (2)$$

where $\mathcal{N}(0, dt \cdot \sigma^2)$ is a normally distributed random variable with mean 0 and variance $dt \cdot \sigma^2$, where σ describes the amount of noise. This standard theoretical approach has previously been applied to a neural model by Brown et al. (2004).

The expression for the oscillatory firing rate can then be introduced into the general autocorrelogram equation, allowing us to obtain an analytical relationship between the parameters of the oscillatory signal (A , B and σ) and the values of the corresponding autocorrelogram. Once this relationship is obtained, we can determine the value of A from the zero value of the autocorrelogram $Corr_{XX}(0)$.

Mathematically, we may represent this as follows. We first consider the general equation of a autocorrelogram:

$$Corr_{XX}(\tau) = \lim_{T \rightarrow \infty} \frac{1}{2T} \int_{-T}^T s(t + \tau) \cdot s(t) dt \quad (3)$$

which, for the case of $\tau = 0$ becomes:

$$Corr_{XX}(0) = \lim_{T \rightarrow \infty} \frac{1}{2T} \int_{-T}^T s^2(t) dt \quad (4)$$

Now we substitute the analytical expression of $s(t)$ (eq. (1)) into this last equation, obtaining:

$$Corr_{XX}(0) = \lim_{T \rightarrow \infty} \frac{1}{2T} \int_{-T}^T (A \sin(t + \phi(t)) + B)^2 dt \quad (5)$$

which, after expanding the squared term, becomes:

$$Corr_{XX}(0) = \lim_{T \rightarrow \infty} \frac{A^2}{2T} \int_{-T}^T \sin^2(t + \phi(t)) dt + \lim_{T \rightarrow \infty} \frac{AB}{T} \int_{-T}^T \sin(t + \phi(t)) dt + \lim_{T \rightarrow \infty} \frac{1}{2T} \int_{-T}^T B^2 dt \quad (6)$$

Note that for a periodic or constant function $f(t)$, $\lim_{T \rightarrow \infty} \frac{1}{2T} \int_{-T}^T f(t) dt$ converges to the average value of $f(t)$. Hence the third integral is easily solved to give:

$$Corr_{XX}(0) = \lim_{T \rightarrow \infty} \frac{A^2}{2T} \int_{-T}^T \sin^2(t + \phi(t)) dt + \lim_{T \rightarrow \infty} \frac{AB}{T} \int_{-T}^T \sin(t + \phi(t)) dt + B^2 \quad (7)$$

Likewise, in the absence of noise the first two integrals would be equal to the average values of the functions $\sin^2$ and $\sin$, which respectively are $1/2$ and 0 . We now show that even in the presence of noise the values of these integrals does not change, and therefore we will be able to solve them by using the same procedure as the one used for the third integral.

Due to the presence of the noise term $\phi(t)$, to solve the first and second integral we have to consider the limit to infinity of the integral boundaries, which implies that we will have to sum an infinite number of sin terms to solve each one of the integrals using Riemann sums. In this situation, given that the Riemann terms are all sin functions with a specific phase θ , what is actually significant is the density of $\sin(\theta)$ terms that there are for each different possible value of $\theta \in [0, 2\pi)$. This value of phase θ is related with the original argument $t + \phi(t)$ of the sine function by the fact that for every $t + \phi(t) \in (-\infty, +\infty)$ there is a corresponding $\theta \in [0, 2\pi)$ such that $\theta + 2\pi N = t + \phi(t)$ for some $N \in \mathbb{N}$, which, in modulo notation, may be written as $\theta \equiv t + \phi(t) \pmod{2\pi}$. To calculate the number of existing $\sin(\theta)$ terms for each possible value of θ , we have to consider the probability distribution of the Wiener process $\phi(t)$, which is equal to $\mathcal{N}(0, t \cdot \sigma^2)$. Since this probability distribution is symmetric, it means that for every sin term with initial argument t , once the noise term $\phi(t)$ is added there will be the same probability of obtaining a sin term with argument $t + \phi(t) > t$ than $t + \phi(t) < t$. In terms of the phase θ , for every of its possible values there is an infinite collection of time points $t_{\theta 1} + \phi_{\theta 1}(t)$, $t_{\theta 2} + \phi_{\theta 2}(t)$, ... $t_{\theta \infty} + \phi_{\theta \infty}(t)$ which give $\theta \equiv t_{\theta i} + \phi_{\theta i}(t) \pmod{2\pi}$ for $i = 1, 2, \dots, \infty$. As the probability distribution of $\phi(t)$ is symmetric and each $t \in \mathbb{R}$ has the same number of time points higher than smaller than t , then this implies that there will be the same number of sin terms for every possible value of the phase $\theta \in [0, 2\pi)$. As with the integral, what is significant is the number of sin terms for each possible value of θ , and this number does not change in the presence of noise, consequently we can suppress the noise terms in these two sin integrals to obtain:

$$Corr_{XX}(0) = \frac{1}{2} A^2 + B^2 \quad (8)$$

as the values of the integral limits converge to the mean value of the periodic functions $\sin^2$ and $\sin$.

This final equation is the one used in this manuscript to extract the oscillatory firing rate amplitude A from an autocorrelogram for a given mean firing rate B of the analysed neuron.

A final remark is that, in the practical situation of an autocorrelogram calculated from a spiky signal (instead of a autocorrelogram calculated from a continuous mean firing rate signal), the effect of the refractory period on the value of $Corr_{XX}(0)$ should be taken into account. In this case, $Corr_{XX}(0)$ has to be approximated by the highest value of $Corr_{XX}(\tau)$ existing outside the refractory period range of the corresponding autocorrelogram. This approximated value tends to appear as two symmetric maximums immediately at both side of the central dip, which is generated by the refractory period. We consider, at least in the case of the studies we use (Bergman et al., 1994; Raz et al., 2000), that the mean value of such two maximums is a good approximation to $Corr_{XX}(0)$.

B The original model exhibits a Hopf bifurcation

The nature of the bifurcation that the original model (eq. 2 of main text) undergoes can be further studied by analysing the roots of the characteristic equation. The bifurcation generates a limit cycle for values of K higher than ~ 0.3 (see section Results), a characteristic feature of Hopf bifurcations. The smooth change of the highest pair of roots as it passes through $\mathbb{R} = 0$ (real part of complex root equal to 0) further confirms the Hopf nature of the bifurcation (see Fig. 1). The transition to oscillations from steady state, unaccompanied by a region of bistability, is a characteristic of a supercritical Hopf bifurcation. Clinical observations of Parkinson's patients (e.g. (Jankovic, 2008)), suggest a similar progression in the appearance of bradykinesia and beta band activity. By this, we mean that there is no apparent region of bistability (accompanied by hysteresis) with the clinical onset of bradykinesia. Whilst patients can show instant moments of rapid movement (i.e. kinesia paradoxa), these are triggered by external cues (such as noise or marching music) which facilitate access to motor programs, only for the duration of the stimulus, rather than a patient showing intermingled periods of normal response and bradykinesia. We should point out that whilst we consider a specific parameter set giving rise to this bifurcation, our analytical conditions identify robust regions of parameter space where such a bifurcation to oscillations occurs.

C Derivation of the non delayed linear model

The linear delayed model was expressed by the following equations (see eq. 5):

$$\begin{cases} \tau \dot{STN}(t) = -w_{GS}GP(t - \Delta t) + w_{CS}Ctx - STN(t) \\ \tau \dot{GP}(t) = w_{SG}STN(t - \Delta t) - w_{GG}GP(t - \Delta t) - w_{XG}Str - GP(t) \end{cases} \quad (9)$$

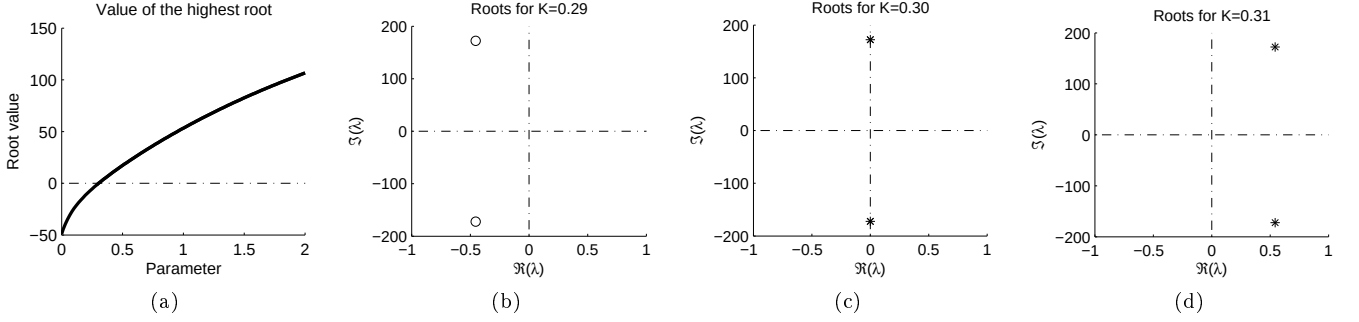


Figure 1: Consideration of the roots of the characteristic equation for the original model (eq. 2). **a**: Value of the highest pair of roots for different values of K . The smooth change of the highest pair can be observed for $K \approx 0.3$. **b**: Highest roots for $K = 0.29$, before the Hopf bifurcation. Roots with negative real part are shown as circles. **c**: Highest roots for $K = 0.3$, close to the Hopf bifurcation. Roots with positive real part are shown as stars. **d**: Highest roots for $K = 0.31$, past the Hopf bifurcation.

This can be further simplified using the Taylor expansion of the delayed terms $GP(t - \Delta t)$ and $STN(t - \Delta t)$. If we consider the Taylor expansion of a function $x(t)$ near a point in time t_0 :

$$x(t) = x(t_0) + \dot{x}(t_0)(t - t_0) + \frac{\ddot{x}(t_0)}{2!}(t - t_0)^2 + \dots \quad (10)$$

then we can use this to approximate a delayed term $x(t_0 - \Delta t)$. Substituting t by $(t_0 - \Delta t)$ in the Taylor series, we obtain:

$$x(t_0 - \Delta t) = x(t_0) - \Delta t \cdot \dot{x}(t_0) + \Delta t^2 \frac{\ddot{x}(t_0)}{2!} - \dots \quad (11)$$

Using the first two terms of the Taylor expansion for $GP(t - \Delta t)$ and $STN(t - \Delta t)$, we obtain the following first order approximation of the non delayed linear model (see eq. 9):

$$\begin{cases} \tau \dot{STN} = -w_{GS}GP + w_{GS}\Delta t \cdot \dot{GP} + w_{CS}Ctx - STN \\ \tau \dot{GP} = w_{SG}STN - w_{SG}\Delta t \cdot \dot{STN} - w_{GG}GP + w_{GG}\Delta t \cdot \dot{GP} - w_{XG}Str - GP \end{cases} \quad (12)$$

In this equation all the terms depend on t . For this reason, the nomenclature has been simplified denoting $STN(t)$ and $GP(t)$ simply as STN and GP .

This system of equations is linear and has no delays, therefore it can be analysed using common linear system techniques. For this, however, it is convenient to express the system in the common normalised form $\dot{x} = A \cdot x$. With this purpose, we first eliminate the time constant τ from (Eq. 12) rescaling time in units of τ . The resulting system of equations is:

$$\begin{cases} \dot{STN} = -w_{GS}GP + w_{GS}\frac{\Delta t}{\tau}\dot{GP} + w_{CS}Ctx - STN \\ \dot{GP} = w_{SG}STN - w_{SG}\frac{\Delta t}{\tau}\dot{STN} - w_{GG}GP + w_{GG}\frac{\Delta t}{\tau}\dot{GP} - w_{XG}Str - GP \end{cases} \quad (13)$$

The second step to obtain the normalised form of the linear undelayed model is to find an expression for the derivatives $\dot{STN}$ and $\dot{GP}$, which does not depend on any other derivative term of the system. To obtain this expression for $\dot{STN}$ we first have to rewrite the second equation of the system (13) in an explicit form for $\dot{GP}$:

$$\dot{GP} = \frac{1}{1 - w_{GG}\frac{\Delta t}{\tau}} \left(w_{SG}STN - w_{SG}\frac{\Delta t}{\tau}\dot{STN} - (1 + w_{GG})GP - w_{XG}Str \right) \quad (14)$$

Now, we can substitute this new expression (14) into the first equation of system (13), obtaining an equation for $\dot{STN}$:

$$\dot{STN} = -w_{GS}GP + \frac{w_{GS}\frac{\Delta t}{\tau}}{1 - w_{GG}\frac{\Delta t}{\tau}} \left(w_{SG}STN - w_{SG}\frac{\Delta t}{\tau}\dot{STN} - (1 + w_{GG})GP - w_{XG}Str \right) + w_{CS}Ctx - STN \quad (15)$$

Now, to obtain its explicit form, we first multiply both sides of the equation by $(1 - w_{GG}\frac{\Delta t}{\tau})$:

$$\begin{aligned} (1 - w_{GG}\frac{\Delta t}{\tau})\dot{STN} = & - (1 - w_{GG}\frac{\Delta t}{\tau})w_{GS}GP + w_{GS}\frac{\Delta t}{\tau} \left(w_{SG}STN - w_{SG}\frac{\Delta t}{\tau}\dot{STN} - (1 + w_{GG})GP - w_{XG}Str \right) \dots \\ & \dots + (1 - w_{GG}\frac{\Delta t}{\tau})w_{CS}Ctx - (1 - w_{GG}\frac{\Delta t}{\tau})STN \end{aligned} \quad (16)$$

And finally we group terms together, moving all those involving $\dot{STN}$ to the left hand side of the equation, giving:

$$\begin{aligned} \left(1 - w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\left(\frac{\Delta t}{\tau}\right)^2 \right)\dot{STN} = & (w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\frac{\Delta t}{\tau} - 1)STN - (w_{GS} + w_{GS}\frac{\Delta t}{\tau})GP - w_{XG}w_{GS}\frac{\Delta t}{\tau}Str \dots \\ & \dots + (1 - w_{GG}\frac{\Delta t}{\tau})w_{CS}Ctx \end{aligned} \quad (17)$$

To obtain an equivalent expression for $\dot{GP}$ we proceed in a similar manner as for $\dot{STN}$. The first equation of system (13) is already an explicit expression for $\dot{STN}$, therefore we can substitute it into the second equation of the same system (13) obtaining:

$$\dot{GP} = w_{SG}STN - w_{SG}\frac{\Delta t}{\tau} \left(-w_{GS}GP + w_{GS}\frac{\Delta t}{\tau}\dot{GP} + w_{CS}Ctx - STN \right) - w_{GG}GP + w_{GG}\frac{\Delta t}{\tau}\dot{GP} - w_{XG}Str - GP \quad (18)$$

Now we group terms together, moving all those involving $\dot{GP}$ to the left hand side of the equation:

$$\begin{aligned} \left(1 + w_{GS}w_{SG} \left(\frac{\Delta t}{\tau}\right)^2 - w_{GG} \frac{\Delta t}{\tau}\right) \dot{GP} = & (w_{SG} + w_{SG} \frac{\Delta t}{\tau}) STN_i + (w_{GS}w_{SG} \frac{\Delta t}{\tau} - w_{GG} - 1) GP - w_{CS}w_{SG} \frac{\Delta t}{\tau} Ctx... \\ & ... - w_{XG} Str \end{aligned} \quad (19)$$

Which is the equivalent final expression of $\dot{GP}$ with no derivatives in the right hand side. Combining the two previously obtained equations for $\dot{STN}$ (Eq. (17)) and $\dot{GP}$ (Eq (19)) we obtain system (13) which is expressed in normalised form:

$$\left\{ \begin{aligned} \left(1 - w_{GG} \frac{\Delta t}{\tau} + w_{SG}w_{GS} \left(\frac{\Delta t}{\tau}\right)^2\right) \dot{STN} = & (-1 + w_{GG} \frac{\Delta t}{\tau} + w_{SG}w_{GS} \frac{\Delta t}{\tau}) STN - w_{GS} \left(\frac{\Delta t}{\tau} + 1\right) GP - w_{XG}w_{GS} \frac{\Delta t}{\tau} Str... \\ & ... + w_{CS} \left(1 - w_{GG} \frac{\Delta t}{\tau}\right) Ctx \\ \left(1 - w_{GG} \frac{\Delta t}{\tau} + w_{SG}w_{GS} \left(\frac{\Delta t}{\tau}\right)^2\right) \dot{GP} = & w_{SG} \left(1 + \frac{\Delta t}{\tau}\right) STN_i + (-1 - w_{GG} + w_{GS}w_{SG} \frac{\Delta t}{\tau}) GP - w_{XG} Str... \\ & ... - w_{CS}w_{SG} \frac{\Delta t}{\tau} Ctx \end{aligned} \right. \quad (20)$$

D Linear non delayed model: dynamics on the boundary

The normalised form of the non delayed linear model (Eq. (20)) obtained in appendix C is valid only when the state of the system (STN, GP) is outside the imposed lower boundaries, $STN = 0$ and $GP = 0$ (i.e. it is valid only when either $STN \neq 0$ or $GP \neq 0$). This is because when $GP = 0$, $\dot{GP}$ cannot be negative, as the firing rate cannot decrease further (the same is true when $STN = 0$) (see Fig 6). However, there are some regions in the axis $GP = 0$ where the value for $\dot{GP}$ defined by eq. (20) becomes negative. An equivalent situation occurs for $STN = 0$, where, in some regions $\dot{STN}$ becomes negative as expressed by eq. (20). The reason for this is that the substitutions of $\dot{GP}$ and $\dot{STN}$ used in eq. (15) and in eq. (18) to obtain the normalised system (20) are not valid in these regions of the boundaries, as such substitutions imply that either $\dot{GP}$ or $\dot{STN}$ can be negative. In these cases the correct substitution that should be used to obtain the normalised system for the boundaries is $\dot{GP} = 0$ or $\dot{STN} = 0$, depending on which boundary the state of the system lies. In summary, equation (20) expresses the flow of the system only outside the lower boundaries, so we now proceed to calculate expressions for the flow inside the boundaries.

To obtain the equation for the boundary $GP = 0$ we first calculate for which regions of the boundary $\dot{GP}$ becomes negative. $\dot{GP} < 0$ if

$$w_{SG} \left(1 + \frac{\Delta t}{\tau}\right) STN + (-1 - w_{GG} + w_{GS}w_{SG} \frac{\Delta t}{\tau}) GP - w_{XG}Str - w_{CS}w_{SG} \frac{\Delta t}{\tau} Ctx < 0 \quad (21)$$

assuming we lie on the $GP = 0$ boundary this becomes:

$$\begin{aligned} w_{SG} \left(1 + \frac{\Delta t}{\tau}\right) STN - w_{XG}Str - w_{CS}w_{SG} \frac{\Delta t}{\tau} Ctx &< 0 \\ STN &< \frac{w_{XG}Str + w_{CS}w_{SG} \frac{\Delta t}{\tau} Ctx}{w_{SG}(1 + \frac{\Delta t}{\tau})} \end{aligned} \quad (22)$$

Which implies that in the $GP = 0$ boundary, and for the values of STN expressed by eq. (22), instead of the substitution $\dot{GP} = w_{SG}STN - w_{SG}\Delta t \cdot \dot{STN} - y - GP$ in step (18) we must use $\dot{GP} = 0$. The substitution in equation (13) to obtain $\dot{STN}$ must therefore be:

$$\begin{aligned} \dot{STN} &= -w_{GS}GP + w_{GS} \frac{\Delta t}{\tau} \dot{GP} + w_{CS}Ctx - STN \\ \dot{STN} &= -w_{GS}(0) + w_{GS} \frac{\Delta t}{\tau} (0) + w_{CS}Ctx - STN \\ \dot{STN} &= w_{CS}Ctx - STN \end{aligned} \quad (23)$$

The same situation happens on the $STN = 0$ boundary, where $\dot{STN}$ can become negative as expressed by eq. (20). Here $\dot{STN} < 0$ if:

$$\begin{aligned} (-1 + w_{GG} \frac{\Delta t}{\tau} + w_{SG}w_{GS} \frac{\Delta t}{\tau}) STN - w_{GS} \left(\frac{\Delta t}{\tau} + 1\right) GP - w_{XG}w_{GS} \frac{\Delta t}{\tau} Str + w_{CS} \left(1 - w_{GG} \frac{\Delta t}{\tau}\right) Ctx &< 0 \\ -w_{GS} \left(\frac{\Delta t}{\tau} + 1\right) GP - w_{XG}w_{GS} \frac{\Delta t}{\tau} Str + w_{CS} \left(1 - w_{GG} \frac{\Delta t}{\tau}\right) Ctx &< 0 \\ GP &> \frac{-w_{XG}w_{GS} \frac{\Delta t}{\tau} Str + w_{CS}Ctx - w_{CS}w_{GG} \frac{\Delta t}{\tau} Ctx}{w_{GS}(1 + \frac{\Delta t}{\tau})} \end{aligned} \quad (24)$$

In this case we should make the substitution $\dot{STN} = 0$ instead of $\dot{STN} = -w_{GS}GP + w_{GS} \frac{\Delta t}{\tau} \cdot \dot{GP} + y - STN$ in step (15) to obtain the value of $\dot{GP}$. Doing this we obtain a new expression of $\dot{GP}$ for this region of the boundary, which is:

$$\begin{aligned} \dot{GP} &= w_{SG}STN - w_{SG} \frac{\Delta t}{\tau} \dot{STN} - w_{GG}GP + w_{GG} \frac{\Delta t}{\tau} \dot{GP} - w_{XG}Str - GP \\ \dot{GP} &= w_{SG}(0) - w_{SG} \frac{\Delta t}{\tau} (0) - w_{GG}GP + w_{GG} \frac{\Delta t}{\tau} \dot{GP} - w_{XG}Str - GP \\ (1 - w_{GG} \frac{\Delta t}{\tau}) \dot{GP} &= -(1 + w_{GG}) GP - w_{XG}Str \end{aligned} \quad (25)$$

However this would imply that GPe firing rate can increase to infinity without any excitatory input if $1 < w_{GG} \frac{\Delta t}{\tau}$. This is an unfortunate artifact of the non delay linear model, which is not present in the linear delayed model (9), where GPe firing rate cannot increase further if STN activity has been zero for a time greater than Δt (or $\frac{\Delta t}{\tau}$ in the units of τ). For this reason it will be more accurate to employ directly the linear delay model (9) in this boundary. This result is (assuming STN firing rate has been 0 for time greater than Δt (or $\frac{\Delta t}{\tau}$ in the units of τ)):

$$\begin{aligned}
\dot{GP}(t) &= w_{SG}STN(t - \frac{\Delta t}{\tau}) - w_{GG}GP(t - \frac{\Delta t}{\tau}) - w_{XG}Str - GP(t) \\
\dot{GP}(t) &= (0) - w_{GG}GP(t - \frac{\Delta t}{\tau}) - w_{XG}Str - GP(t) \\
\dot{GP}(t) &= -w_{GG}GP(t - \frac{\Delta t}{\tau}) - w_{XG}Str - GP(t)
\end{aligned} \tag{26}$$

Summarising the system when on the boundary $GP = 0$ is defined by the following inequalities, where the boundaries intersect with the nulclines of the system:

$$\left\{ \begin{array}{l} \text{if } STN \geq \frac{w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx}{w_{SG}(1 + \frac{\Delta t}{\tau})} \\ \text{if } STN < \frac{w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx}{w_{SG}(1 + \frac{\Delta t}{\tau})} \end{array} \right\} \left\{ \begin{array}{l} \left(1 - w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\left(\frac{\Delta t}{\tau}\right)^2\right) \dot{STN} = (-1 + w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\frac{\Delta t}{\tau}) STN... \\ \dots - w_{GS}\left(\frac{\Delta t}{\tau} + 1\right) GP - w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + w_{CS}\left(1 - w_{GG}\frac{\Delta t}{\tau}\right)Ctx \\ \left(1 - w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\left(\frac{\Delta t}{\tau}\right)^2\right) \dot{GP} = w_{SG}\left(1 + \frac{\Delta t}{\tau}\right) STN_i... \\ \dots + (-1 - w_{GG} + w_{GS}w_{SG}\frac{\Delta t}{\tau}) GP - w_{XG}Str - w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx \\ \dot{STN} = w_{CS}Ctx - STN \\ \dot{GP} = 0 \end{array} \right. \tag{27}$$

and similarly on the boundary $STN = 0$

$$\left\{ \begin{array}{l} \text{if } GP \leq \frac{-w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + (w_{CS} - w_{CS}w_{GG}\frac{\Delta t}{\tau})Ctx}{w_{GS}(1 + \frac{\Delta t}{\tau})} \\ \text{if } GP > \frac{-w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + (w_{CS} - w_{CS}w_{GG}\frac{\Delta t}{\tau})Ctx}{w_{GS}(1 + \frac{\Delta t}{\tau})} \end{array} \right\} \left\{ \begin{array}{l} \left(1 - w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\left(\frac{\Delta t}{\tau}\right)^2\right) \dot{STN} = ... \\ \dots (-1 + w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\frac{\Delta t}{\tau}) STN - w_{GS}\left(\frac{\Delta t}{\tau} + 1\right) GP... \\ \dots - w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + w_{CS}\left(1 - w_{GG}\frac{\Delta t}{\tau}\right)Ctx \\ \left(1 - w_{GG}\frac{\Delta t}{\tau} + w_{SG}w_{GS}\left(\frac{\Delta t}{\tau}\right)^2\right) \dot{GP} = w_{SG}\left(1 + \frac{\Delta t}{\tau}\right) STN_i + ... \\ \dots (-1 - w_{GG} + w_{GS}w_{SG}\frac{\Delta t}{\tau}) GP - w_{XG}Str - w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx \\ \dot{STN} = 0 \\ \dot{GP} = -w_{GG}GP(t - \frac{\Delta t}{\tau}) - w_{XG}Str - GP \end{array} \right. \tag{28}$$

E Conditions for the existence of an unstable, clockwise spiral flow:

Having calculated the normalised form of the linear non delayed model (eq. 20) on appendix C, we can write down the stability matrix A as follows:

$$A = \begin{bmatrix} (-1 + w_{GG} \frac{\Delta t}{\tau} + w_{SG} w_{GS} \frac{\Delta t}{\tau}) & -w_{GS} (\frac{\Delta t}{\tau} + 1) \\ w_{SG} (1 + \frac{\Delta t}{\tau}) & (-1 - w_{GG} + w_{GS} w_{SG} \frac{\Delta t}{\tau}) \end{bmatrix} \quad (29)$$

as this is the Jacobian of system (20), which describes the system for $GP > 0$ and $STN > 0$.

The stability of a steady state can be determined by calculating the eigenvalues of the matrix A (eq. 29). Calculating the eigenvalues of our matrix A we obtain:

$$\lambda_{1,2} = r \pm \frac{1}{2} \sqrt{c} \quad (30)$$

where :

$$\begin{aligned} r &= -1 + w_{GG} \frac{\Delta t}{2\tau} - w_{GG} \frac{1}{2} + w_{SG} w_{GS} \frac{\Delta t}{\tau} \\ c &= w_{GG}^2 + 2w_{GG}^2 \frac{\Delta t}{\tau} + w_{GG}^2 \left(\frac{\Delta t}{\tau}\right)^2 - 4w_{SG} w_{GS} - 8w_{SG} w_{GS} \frac{\Delta t}{\tau} - 4w_{SG} w_{GS} \left(\frac{\Delta t}{\tau}\right)^2 \end{aligned} \quad (31)$$

For the system to have an unstable spiral, both eigenvalues should be imaginary with positive real part.

Both eigenvalues will be imaginary if:

$$w_{GG}^2 < 4w_{SG} w_{GS} \quad (32)$$

since $\sqrt{c}$ will be a complex number (weights and delays are always positive or zero) if this condition is held.

Likewise the real part of the roots (r) will be positive if:

$$\begin{aligned} -1 + w_{GG} \frac{\Delta t}{2\tau} - w_{GG} \frac{1}{2} + w_{SG} w_{GS} \frac{\Delta t}{\tau} &> 0 \\ 2w_{SG} w_{GS} \frac{\Delta t}{\tau} &> 2 - w_{GG} \frac{\Delta t}{\tau} + w_{GG} \\ w_{SG} w_{GS} \frac{\Delta t}{\tau} &> 1 + w_{GG} \left(1 - \frac{\Delta t}{\tau}\right) / 2 \end{aligned} \quad (33)$$

The direction of the flow (clockwise or anticlockwise) is also important for the creation a limit cycle with the boundaries, as it is a necessary condition that both of them have the flow in the same angular direction. The flow in the boundaries for the linear non delayed model is clockwise (see supplementary material D and Fig 6), therefore the flow in the rest of the phase portrait should follow the same direction for a limit cycle to be formed. This condition can be demonstrated using the mathematical concept of curl in a vector field. For a three-dimensional vector field (F_x, F_y, F_z) , the curl is defined as:

$$\vec{\nabla} \times \vec{F} = \begin{vmatrix} \vec{i} & \vec{j} & \vec{k} \\ \frac{\delta}{\delta x} & \frac{\delta}{\delta y} & \frac{\delta}{\delta z} \\ F_x & F_y & F_z \end{vmatrix} = \left(\frac{\delta F_z}{\delta y} - \frac{\delta F_y}{\delta z} \right) \vec{i} + \left(\frac{\delta F_x}{\delta z} - \frac{\delta F_z}{\delta x} \right) \vec{j} + \left(\frac{\delta F_y}{\delta x} - \frac{\delta F_x}{\delta y} \right) \vec{k} \quad (34)$$

That applied to our two-dimensional vector field $(\dot{GP}, \dot{STN}, 0)$, is:

$$\vec{\nabla} \times \vec{F} = \begin{vmatrix} \vec{i} & \vec{j} & \vec{k} \\ \frac{\delta}{\delta GP} & \frac{\delta}{\delta STN} & \frac{\delta}{\delta z} \\ \dot{GP} & \dot{STN} & 0 \end{vmatrix} = \left(\frac{\delta 0}{\delta STN} - \frac{\delta \dot{GP}}{\delta z} \right) \vec{i} + \left(\frac{\delta \dot{STN}}{\delta z} - \frac{\delta 0}{\delta GP} \right) \vec{j} + \left(\frac{\delta \dot{STN}}{\delta GP} - \frac{\delta \dot{GP}}{\delta STN} \right) \vec{k} =$$

$$0 \vec{i} + 0 \vec{j} + \left(-w_{GS} \left(\frac{\Delta t}{\tau} + 1 \right) - w_{SG} \left(1 + \frac{\Delta t}{\tau} \right) \right) \vec{k}$$
(35)

Since the quantity multiplying $\vec{k}$ is negative (as the weights and delays are always positive quantities), the flow in the $(\vec{i}, \vec{j})$ plane (i.e. the (GP, STN) plane) is clockwise (from the right hand rule of vectorial calculus).

F Conditions for a sliding boundary

If the flow in the phase portrait of system (6) is an unstable spiral, all trajectories of the system will intersect in some moment with one of the lower boundaries $STN = 0$ or $GP = 0$. Once the state of the system is in one of such boundaries, the flow can continue being indefinitely inside the boundary or abandons it. If it abandons the boundary, the state will incorporate into one of the spiral trajectories, which will intersect again one of the two boundaries at some point in the future. This situation will create a limit cycle composed of 1 or 2 spiral trajectories section and 1 or 2 boundary regions (see Fig. 2). Given the spiral flow of the phase portrait is clockwise (see Appendix E for demonstration), this will happen in four different scenarios (see Fig 2):

- If the steady state is “near” to the $GP = 0$ boundary, the limit cycle will be composed by a section of the $GP = 0$ boundary and a spiral path departing from this boundary and intersecting it an an earlier point. (see Fig. 2a)
- If the steady state is “near” to the $STN = 0$ boundary, the limit cycle will be composed by a section of the $STN = 0$ boundary and a spiral path departing from this boundary and intersecting it an an earlier point. (see Fig. 2b)
- If the steady state is a “similar” distance from both boundaries the limit cycle will be composed by a section of both boundaries and a spiral trajectory concocting $GP = 0$ with $STN = 0$. (see Fig. 2c)
- If the steady state is at a “similar” distance from both boundaries the limit cycle will be composed by a section of both boundaries and two spiral trajectories, one connecting $GP = 0$ with $STN = 0$ and other connecting $STN = 0$ with $GP = 0$. (see Fig. 2d)

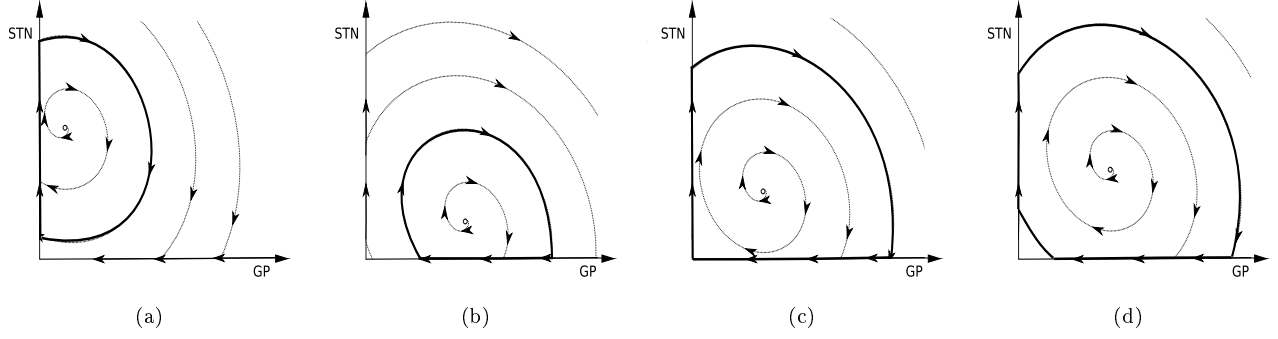


Figure 2: The four cases of limit cycle creation. The four cases of creation of a limit cycle in the approximation system (6). The dashed lines show the direction of the flow in the phase portrait. The bold closed trajectory is the created limit cycle. **a**: If the steady state is near the $GP = 0$ boundary. **b**: If the steady state is near the $STN = 0$ boundary. **c** and **d**: If the steady state is at a similar distance from both boundaries.

The only manner in which this limit cycle could not be created, is if the state of the system never leaves the boundaries. This could happen only if there exists a steady state in one of the boundaries, or if the state tends to infinity in some boundary without abandoning it.

The system in the boundaries was calculated in Appendix C eq. (28) for $STN = 0$ boundary and eq. (27) for $GP = 0$ boundary.

This determines the direction of the flow in the boundaries. This direction, together with the direction in the phase portrait, can be seen in Fig. 6. In the boundary $GP = 0$ it is:

$$\left\{ \begin{array}{l} \text{if } STN \geq \frac{w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx}{w_{SG}(1+\frac{\Delta t}{\tau})} \\ \text{if } STN < \frac{w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx}{w_{SG}(1+\frac{\Delta t}{\tau})} \end{array} \right\} \left\{ \begin{array}{l} \dot{STN} > 0 \\ \dot{GP} > 0 \\ \dot{STN} \rightarrow w_{CS}Ctx \\ \dot{GP} = 0 \end{array} \right. \quad (36)$$

and in the boundary $STN = 0$:

$$\left\{ \begin{array}{l} \text{if } GP \leq \frac{-w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + w_{CS}Ctx - w_{CS}w_{GG}\frac{\Delta t}{\tau}Ctx}{w_{GS}(1+\frac{\Delta t}{\tau})} \\ \text{if } GP > \frac{-w_{XG}w_{GS}\frac{\Delta t}{\tau}Str + w_{CS}Ctx - w_{CS}w_{GG}\frac{\Delta t}{\tau}Ctx}{w_{GS}(1+\frac{\Delta t}{\tau})} \end{array} \right\} \left\{ \begin{array}{l} \dot{STN} > 0 \\ \dot{GP} < 0 \\ \dot{STN} = 0 \\ \dot{GP} < 0 \end{array} \right. \quad (37)$$

Hence for the $STN = 0$ boundary, the flow never tends to infinity, nor to any steady state on the boundary, since none exist. On the $GP = 0$ boundary the flow also never tends to infinity but, there is a steady state at

$STN = y$ if

$$w_{CS}Ctx < \frac{w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx}{w_{SG}\left(1 + \frac{\Delta t}{\tau}\right)} \quad (38)$$

which is equivalent to:

$$\begin{aligned} \left(1 + \frac{\Delta t}{\tau}\right)w_{SG}w_{CS}Ctx &< w_{XG}Str + w_{CS}w_{SG}\frac{\Delta t}{\tau}Ctx \\ w_{SG}w_{CS}Ctx &< w_{XG}Str \end{aligned} \quad (39)$$

In summary, the flow in the boundaries will connect different trajectories (or the same trajectory with itself) except when (40) is true. Thus a limit cycle will be created when:

$$w_{SG}w_{CS}Ctx < w_{XG}Str \quad (40)$$

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