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Modulating the oscillations produced by discrete biological models

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Abstract—An analytical approach is developed to modulate either the frequency or the amplitude of an oscillator. We present the strategy in general two-dimensional discrete polynomial systems undergoing the Neimark-Sacker bifurcation imposed by designed linear feedback controls, and apply the method to a model of an ideal storage system and the Chialvo neuronal model. Our method shows potential to understand the mechanism of frequency and amplitude modulations in various biological systems.

1. Introduction

Oscillations are omnipresent in real world and particularly in biological systems: from signalling pathways such as NFκB oscillations, to rhythmic clocks both in animals and plants, and to hibernation [1, 2]. In the cell cyclic oscillation model, the period of the cell cycle ranges from about 10 minutes in rapidly dividing embryos to tens of hours in dividing somatic cells, while the variation in the amplitude of the oscillation seems neither necessary nor desirable [3]: a typical example of frequency modulation (FM) [4]. In the hippocampus or the inferior-temporal cortex in the brain, the amplitude of the theta wave (4-8Hz) increases after learning, without affecting the frequency: a typical example of amplitude modulation (AM) [5, 6]. There is accumulated evidence that biological systems (e.g. gene regulation, neuronal networks etc) use either FM or AM to encode and decode information. Therefore, an interesting question is how FM or AM can be achieved for an oscillator. This issue has attracted a lot of interests and has recently been discussed in the literature for many biological oscillator models [7], yet all based upon numerical simulations and for FM exclusively.

Here we present a theoretical approach to tackle this question. Specifically, we consider a general two-dimensional discrete polynomial system undergoing the well-known Neimark-Sacker bifurcation with the change of a bifurcation parameter. By comparing the normal forms of this system with and without a linear feedback control, analytical forms of the feedback for FM and AM can be obtained. This approach allows for explicitly modulating the the oscillator and creates the possibility to study the configurations in the feedback gain matrix for FM and AM. For example, we might be able to understand from a theoretical perspective why both negative and positive feedback loops play essential roles in modulating oscillators, as reported in the literature [7].

2. Methods

Consider a general two-dimensional discrete polynomial model:

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \mapsto \begin{bmatrix} G_1(x_1, x_2; \gamma) \\ G_2(x_1, x_2; \gamma) \end{bmatrix} + O(\|\boldsymbol{x}\|^4), \qquad (1)$$

where $G_i(x_1, x_2; \gamma) = \sum_{k+l\leqslant 3;\ k,l\geqslant 0} g^i_{kl}(\gamma) x_1^k x_2^l, i = 1, 2$, are polynomials with degrees no higher than 3, γ is a scalar parameter. Suppose the system has a unique fixed point. Then without loss of generality the fixed point can be set at the origin by a simple parameter-dependent coordinate shift. This is assumed in the following, from which the constant terms in $G_i(x_1, x_2; \gamma), i = 1, 2$ vanish. We further assume that the fixed point of the system undergoes the supercritical Neimark-Sacker bifurcation at some parameter value $\gamma = \gamma^*$, and the system (1) exhibits oscillating behaviors. Adding linear feedback loops to the system (1)

$$\begin{bmatrix} x_1 \to x_1 & x_2 \to x_1 \\ x_1 \to x_1 & x_2 \to x_2 \end{bmatrix} = \begin{bmatrix} c & d \\ e & f \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix}, \qquad (2)$$

where $x_i \to x_j$ denotes the feedback from x_i to x_j, $i, j = 1, 2$; c, d, e and f are feedback feedback gains, the original system can be reorganized as follows:

$$\boldsymbol{x} \mapsto \boldsymbol{A}(\gamma)\boldsymbol{x} + \boldsymbol{G}(\boldsymbol{x}, \gamma) + O(\|\boldsymbol{x}\|^4), \qquad (3)$$

where

$$\boldsymbol{A}(\gamma) = \begin{bmatrix} g^1_{10} + c & g^1_{01} + d \\ g^2_{10} + e & g^2_{01} + f \end{bmatrix}, \qquad (4)$$

and $\boldsymbol{G}(\boldsymbol{x}, \gamma)$ summaries all the quadratic and cubic terms. We then intend to design the combinations of the feedback gains c, d, e and f such that the amplitude (or frequency) of the linear controlled system (3) remains unchanged while the frequency (or amplitude) changes as feedback gains vary, which corresponds to FM (or AM).

The first step towards this is to ensure that the controlled system also undergoes the Neimark-Sacker bifurcation at $\gamma = \gamma^*$, and therefore exhibits oscillating behaviors. This requires the existence of a pair of complex eigenvalues $\mu_{1,2}(\gamma) = r(\gamma)e^{\pm i\phi(\gamma)}$ for the Jacobian matrix $\boldsymbol{A}(\gamma)$ and the multipliers are on the unit circle at the bifurcation point $\gamma = \gamma^*$. This is equivalent to $\Delta(\gamma^*) < 0$ and

$r^2(\gamma^*) = \det\left[\boldsymbol{A}(\gamma^*)\right] = 1$, where $\Delta(\gamma)$ is the discriminant for the polynomial $\det\left[\lambda\boldsymbol{I} - \boldsymbol{A}(\gamma)\right]$. Once this is satisfied, systems with and without linear feedback control can be transformed into normal forms when the parameter γ is close to the bifurcation point γ^* via an invertible coordinate and parameter change. In the complex domain, the normal form reads

$$w \mapsto \mu w + \lambda w^2 \bar{w} + O(|w|^4), \tag{5}$$

where w is a complex variable, $\mu = \mu(\gamma) = r(\gamma)e^{i\phi(\gamma)}$, λ is a function of the bifurcation parameter γ and depends on the feedback gains. By further imposing conditions on $\chi(\gamma) = \mathrm{Re}\left[e^{-i\phi(\gamma)}\lambda(\gamma)\right]$, the system (3) undergoes a supercritical Neimark-Sacker bifurcation at $\gamma = \gamma^*$. A stable closed invariant curve bifurcates from the fixed point when γ passes through γ^*. Indeed, the amplitude and frequency of the oscillator can be explicitly computed. The radius of the invariant curve is represented by a function of γ, denoted by, $\hat{r}(\gamma)$, and the rotation angle is approximately $\phi(\gamma)$.

Having obtained the normal forms, it is then straightforward to design the linear feedback control to achieve FM or AM. Specifically, for FM, it is required that the amplitude of the stable closed invariant curve bifurcates from the fixed point remains unchanged with and without linear feedback control, which leads to

$$\hat{r}(\gamma) = \hat{r}(\gamma)\Big|_{c=d=e=f=0}. \tag{6}$$

By altering the feedback weights c, d, e and f under this condition, the amplitude of the oscillator will remain approximately unchanged while the frequency can be modulated. Similarly, for FM, it is required that

$$\phi(\gamma) = \phi(\gamma)\Big|_{c=d=e=f=0}. \tag{7}$$

which can be simplified to

$$\frac{g_{10}^1 + g_{01}^2 + c + f}{r(\gamma)} = \frac{g_{10}^1 + g_{01}^2}{\sqrt{g_{10}^1 g_{01}^2 - g_{10}^2 g_{01}^1}}. \tag{8}$$

By altering the feedback weights c, d, e and f under this condition, the frequency of the oscilltor will remain approximately unchanged while the amplitude can be modulated.

3. Examples

To validate the practical usefulness of our theoretical findings for two-dimensional discrete dynamical systems, we apply our method to two representative models of physical and biological significance.

3.1. Example 1 - An ideal storage system

The first example is a rather simple system in which some substance is being stored, released, and replenished simultaneously in some interdependent way [8]. The dynamics of the system is described by a two-dimensional map-based discrete-time model which takes the form

$$\begin{bmatrix} u_1 \\ u_2 \end{bmatrix} \mapsto \begin{bmatrix} u_1 - u_1 u_2 + \gamma \\ f(u_1 u_2) \end{bmatrix}, \tag{9}$$

where γ is a positive constant and f is a monotonically increasing function defined on $\mathbb{R}^+ := [0, +\infty]$, whose range is contained in the interval $(0, 1)$. It follows from the equations that the system has a unique fixed point $\mathcal{E}(\gamma) = \left[\gamma/f(\gamma), f(\gamma)\right]^T$. By a simple parameter-dependent coordinate shift $\boldsymbol{x} = \boldsymbol{u} - \mathcal{E}(\gamma)$, the fixed point can be set at the origin. According to [8], if the map f is two times differentiable, $\gamma f'(\gamma) = f(\gamma)$ holds for $\gamma = \gamma^*$, and that γ^* is not an inflexion point of f, i.e., $f''(\gamma^*) \neq 0$ stands, then, as γ passes through γ^*, the origin of the model changes its stability and a unique closed invariant curve bifurcates from the fixed point. Therefore, we can add linear feedback to the system and apply the theory established above to modulate the frequency and amplitude of the oscillator. The feedback considered here takes a particular form by setting $c = f$. To visualize the results, we specify $f(\gamma)$ as a sigmoidal function of the form proposed in [8]:

$$f_{\kappa,\mu}(\gamma) = \frac{1}{1 + e^{-\kappa(\gamma-\mu)}}, \tag{10}$$

with $\kappa = 5$ and $\mu = 0.5$. These settings ensure the occurrence of the Neimark-Sacker bifurcation in the original system. The controlled system was simulated with $\gamma = \gamma^* + 10^{-4}$. When the linear feedback control vanishes, i.e., $c = d = e = 0$, the system coincides with the original system and has an amplitude of approximately 0.0220 and the rotation angle of the invariant curve is 0.486.

For AM, the feasible values of c, d and e were searched in the interval $[-1, 1]$ with a step length 10^{-3}. Fig. 1 shows the numerical results of AM. In both panels, the blue lines correspond to the first component of the original system. It can been seen that the numerical results fit the theory quite well and more crucially, with appropriate linear feedback controls, the amplitude of the original system can either increase (red line in the left panel) or decrease (green line in the right panel).

For FM, optimal values of c, d and e were also numerically searched in the interval $[-1, 1]$ with a step length 10^{-3}. Fig. 2 shows the numerical results of FM. In both panels, the blue lines correspond to the first component of the original system. It can been seen that with appropriate linear feedback controls, the frequency of the original system can either increase (red line in the left panel) or decrease (green line in the right panel).

3.2. Example 2 - The Chialvo neuronal model

For the second example, consider the Chialvo model [9] described by the following system:

$$\begin{bmatrix} u_1 \\ u_2 \end{bmatrix} \mapsto \begin{bmatrix} u_1^2 e^{u_2 - u_1} + \sigma \\ \alpha u_2 - \gamma u_1 + \beta \end{bmatrix}, \tag{11}$$

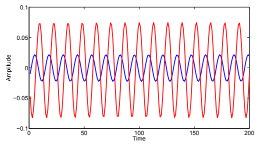

Figure 1: **Amplitude modulation of the storage model**. The parameters are selected as $\kappa = 5, \mu = 0.5, c = f$ and $\gamma = \gamma^* + 10^{-4}$. In both panels, the blue lines correspond to the first component of the original system with a theoretical amplitude approximately 0.0220. (Left panel) The amplitude increases with linear feedback $c = f = 0.0010, d = -0.9790, e = -0.0960$ (red line). (Right panel) The amplitude decreases with linear feedback $c = f = 0, d = 0.2270, e = 0.0520$ (green line).

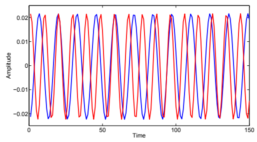

Figure 2: **Frequency modulation of the storage model**. The parameters are selected as $\kappa = 5$, $\mu = 0.5$, $c = f$ and $\gamma = 10^{-4}$. In both panels, the blue lines correspond to the first component of the original system with a theoretical amplitude approximately 0.0220. (Left panel) The frequency increases with linear feedback $c = f = -0.0940, d = 0.0750, e = 0.1650$ (red line). (Right panel) The frequency decreases with linear feedback $c = f = 0.1090, d = 0.8440, e = -0.1090$ (green line).

where u_1 and u_2 represent, respectively, the activation and the recovery variables. The model includes four parameters σ, α, β and γ. In the activation variable, the parameter σ acts as a constant bias. The dynamics of the recovery variable is determined by three positive parameters: the time constant of recovery $\alpha < 1$; the activation-dependence of the recovery process $\gamma < 1$; and the offset β [9]. The Chialvo neuron is intended as a model of excitable dynamics and could display a wide array of dynamical features, including subthreshold oscillations, bistability and chaotic orbits.

Given the above parameter settings along with $\beta \ll 1$, the system has a unique fixed point $\mathcal{E}(\gamma)$, whose coordinate, $[u_1^*(\gamma), u_2^*(\gamma)]$, satisfies the following equations:

$$\begin{cases} u_1^* = u_1^{*2} e^{u_2^* - u_1^*} + \sigma, \\ u_2^* = \alpha u_2^* - \gamma u_1^* + \beta. \end{cases} \quad (12)$$

After a parameter-dependent coordinate shift $\boldsymbol{x} = \boldsymbol{u} - \mathcal{E}(\gamma)$, the fixed point can be set at the origin. Thus the above system (11) can be transformed into

$$\begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \mapsto \begin{bmatrix} (x_1 + u_1^*)^2 e^{x_2 - x_1 + u_2^* - u_1^*} + \sigma - u_1^* \\ \alpha x_2 - \gamma x_1 + (\alpha - 1) u_2^* - \gamma u_1^* + \beta \end{bmatrix}. \quad (13)$$

It can be verified that when α is close to 1, the model (13) undergoes the Neimark-Sacker bifurcation at γ^*, where γ^* satisfies the following equation:

$$\alpha u_1^* (2 - u_1^*) e^{u_2^* - u_1^*} + \gamma^* u_1^{*2} e^{u_2^* - u_1^*} = 1. \quad (14)$$

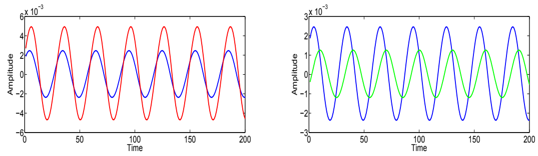

Figure 3: **Amplitude modulation of the Chialvo model**. The parameters are selected as $\gamma = \gamma^* - 10^{-4}$, $\alpha = 0.9$, $\beta = 0.28$ and $\sigma = 0.04$. In both panels, the blue lines correspond to the first component of the original system with a theoretical amplitude approximately 0.0024. (Left panel) The amplitude increases with linear feedback $c = f = 0, d = 0.046, e = 0.479$ (red line). (Right panel) The amplitude decreases with linear feedback $c = f = 0, d = -0.033, e = -1.990$ (green line).

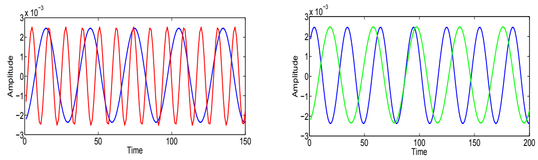

Figure 4: **Frequency modulation of the Chialvo model**. The parameters are selected as $\gamma = \gamma^* - 10^{-4}$, $\alpha = 0.9$, $\beta = 0.28$ and $\sigma = 0.04$. In both panels, the blue lines correspond to the first component of the original system with a theoretical amplitude approximately 0.0024. (Left panel) The frequency increases with linear feedback $c = f = -0.124, d = 0.378, e = 0.347$ (red line). (Right panel) The frequency decreases with linear feedback $c = f = 0.009, d = -0.015, e = 0.081$ (green line).

We still specified $c = f$ in the feedback gains in this example. By intensive computation of the normal form, we obtained the conditions for both FM and AM. Numerical simulations were carried out to verify the theories established above. According to [10], the system was simulated with $\gamma = \gamma^* - 10^{-4}$, $\alpha = 0.9, \beta = 0.28$ and $\sigma = 0.04$. When the linear feedback control vanishes, i.e., $c = d = e = 0$, the system coincides with the original system. The amplitude and the rotation angle of the oscillator are approximately 0.0024 and 0.209 respectively under the above parameter setting.

Fig. 3 shows the numerical results of AM. In both panels, the blue lines correspond to the first component of the original system. It can been seen that the numerical results fit the theory quite well and more crucially, with appropriate linear feedback controls, the amplitude of the original system can either increase (red line in the left panel) or decrease (green line in the right panel).

Fig. 4 shows the numerical results of FM. In both panels, the blue lines correspond to the first component of the original system. It can been seen that with appropriate linear feedback controls, the frequency of the original system can either increase (red line in the left panel) or decrease (green line in the right panel).

The normal form theory is only valid when the bifurcation parameter is sufficiently close to the critical point. This might impede the applications of the proposed analytic ap-

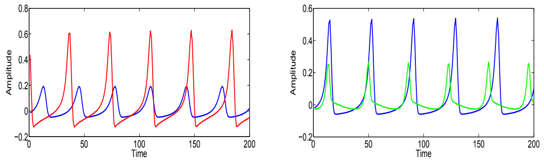

Figure 5: **Amplitude modulation of the Chialvo model**. (Left panel) With the parameters selected as $\gamma = \gamma^* - 0.1$, $\alpha = 0.91$, $\beta = 0.28$ and $\sigma = 0.04$, the amplitude increases with linear feedback $c = f = 0, d = 0.046, e = 0.479$ (red line). (Right panel) With the parameters selected as $\gamma = \gamma^* - 0.1$, $\alpha = 0.90$, $\beta = 0.28$ and $\sigma = 0.04$, the amplitude decreases with linear feedback $c = f = 0, d = -0.033, e = -1.990$ (green line).

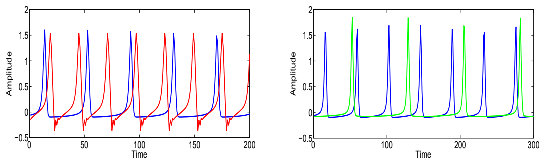

Figure 6: **Frequency modulation of the Chialvo model**. (Left panel) With the parameters selected as $\gamma = \gamma^* - 0.15$, $\alpha = 0.89$, $\beta = 0.28$ and $\sigma = 0.04$, the frequency increases with linear feedback $c = f = -0.124, d = 0.378, e = 0.347$ (red line). (Right panel) With the parameters selected as $\gamma = \gamma^* - 0.1$, $\alpha = 0.89$, $\beta = 0.267$ and $\sigma = 0.04$, the frequency decreases linear feedback $c = f = 0.009, d = -0.015, e = 0.081$ (green line).

proach since real biological systems often display periodic behaviors far from the fixed point. However, Fig. 5 and 6 show that the feedback controls designed near the bifurcation point are still very instructive when the bifurcation parameter is far from the bifurcation point with which the system displays a typical spiking dynamics.

4. Conclusion

In this paper, we have presented an analytical approach to achieve both FM and AM in oscillators modelled by two-dimensional discrete dynamical systems. By computing the normal form of the Neimark-Sacker bifurcation, the amplitude and the frequency of the oscillator can be explicitly obtained and appropriate linear feedback control can be designed. We anticipate that our approach may represent a general principle to engineer biological oscillators, which plays a central role in synthetic biology. Future works include a more careful investigation of the configurations in the feedback gain matrix with biological interpretations. The idea in the present paper can also be extended to engineering oscillators in systems with nonlinear feedbacks, feedback loops or time delays.

Acknowledgments

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