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Cholinergic top-down modulation based on the free-energy principle

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Abstract: Acetylcholine (ACh) has a key role in the cortex in perception. Although cholinergic modulations have been revealed in recent experimental studies, it remains unclear what is the essential role of ACh. In order to clarify the crucial computational function of ACh in perceptual inference, we propose a model of cholinergic top-down modulation based on the free-energy principle in this paper. We made the only assumption that ACh modulates the magnitude of top-down processing. Then, dynamics of the ACh level is derived by the free-energy principle. Our model suggests that ACh reports uncertainty of top-down information and reduces noise of top-down input. Thus, ACh can contribute to precise perception.

Keywords: neuromodulation, acetylcholine, free-energy principle, perception

1 INTRODUCTION

Acetylcholine (ACh) is one of the neuromodulators such as dopamine, serotonin, and noradrenaline. ACh is synthesized in the basal forebrain including medial septum, diagonal band of Broca, and nucleus basalis. Then, it is delivered to large areas of the cortex. Delivered ACh acts various functions in the cortex [3], [4]. First, recurrent intracortical connections and top-down processing are suppressed via muscarinic receptors. Second, afferent input is facilitated via nicotinic receptors. These cholinergic modulations relate to perception.

In theoretical studies, Yu and Dayan have suggested that the ACh level represents the uncertainty associated with top-down information [6], [7]. They proposed an ACh model by means of hidden Markov model, showing that cholinergic modulation leads to efficient perceptual inference. On the other hand, Friston has recently suggested that perception is realized by the free-energy principle. The free-energy principle has strong impacts because we can uniformly deal with neuronal activity, synaptic plasticity, and neuromodulation.

Although cholinergic modulation is well studied in recent studies, the relationship between cholinergic modulation and the free-energy principle is not clear. Furthermore, the crucial computational role of ACh is poorly understood. Here, we propose a model of cholinergic modulation based on the free-energy principle in this paper. We assume that ACh modulates the efficacy of top-down processing, showing that the ACh level changes in response to uncertainty of top-down information and ACh yields better perceptual inference.

2 MODELING OF PERCEPTION

Before we introduce cholinergic modulation, we review the perception model derived by the free-energy principle proposed by Friston [1] in this section. See [1] and [2] for details.

2.1 Generative model

Consider the following state-space model,

$$\dot{x} = Ax + Bv + z_x, \tag{1}$$
$$y = Cx + z_y, \tag{2}$$

where v, x, and y denote input, state, and output, respectively. State equation (1) demonstrates the transition of state x in terms of input v, state itself x, and noise z_x. Output equation (2) defines output y by state x and noise z_y. A, B, and C are time-invariant matrices. This linear state-space model generates observable consequence y by causes x and v. In this sense, this state-space model is called a generative model.

Next, generalized coordinates are introduced under the smoothness assumptions. We assume that all variables are smooth enough to differentiate infinitely. We use the notations, tildes, in the sense of generalized coordinates, e.g., $\tilde{x} := [x^T, \dot{x}^T, \ddot{x}^T, \ldots]^T$. Then, the state-space model can be written by

$$D\tilde{x} = \tilde{A}\tilde{x} + \tilde{B}\tilde{v} + \tilde{z}_x, \tag{3}$$
$$\tilde{y} = \tilde{C}\tilde{x} + \tilde{z}_y, \tag{4}$$

$$\tilde{A} := I \otimes A,\ \tilde{B} := I \otimes B,\ \tilde{C} := I \otimes C, \tag{5}$$
$$D := \begin{bmatrix} 0 & 1 & 0 & \cdots \\ 0 & 0 & 1 & \cdots \\ \vdots & \vdots & & \ddots \end{bmatrix} \otimes I, \tag{6}$$

where I is the identity matrix and $\otimes$ is Kronecker product.

Moreover, if we assume that noises $\tilde{z}_x$ and $\tilde{z}_y$ obey Gaussian distributions $\mathcal{N}(0, \Sigma_x)$ and $\mathcal{N}(0, \Sigma_y)$, we can rewrite the state-space model to the probabilistic model as follows

$$p(\tilde{y}, \tilde{x}, \tilde{v}) = p(\tilde{y}|\tilde{x}, \tilde{v})p(\tilde{x}|\tilde{v})p(\tilde{v}), \tag{7}$$

$$p(\tilde{y}|\tilde{x}, \tilde{v}) = \mathcal{N}(\tilde{y} : \tilde{C}\tilde{x}, \Sigma_y), \tag{8}$$

$$p(\tilde{x}|\tilde{v}) = \mathcal{N}(D\tilde{x} : \tilde{A}\tilde{x} + \tilde{B}\tilde{v}, \Sigma_x). \tag{9}$$

We solve the inversion of this generative model in the following section.

2.2 Perception model

In the perception model, the brain estimates states $\tilde{x}$ and $\tilde{v}$ by observing $\tilde{y}$ and using prior knowledge $\tilde{v}_{\mathrm{pr}}$. Under the ergodic assumptions, given model m, the entropy of sensory state is

$$H(\tilde{y}|m) = -\int p(\tilde{y}|m) \ln p(\tilde{y}|m) d\tilde{y} \tag{10}$$

$$= -\int \ln p(\tilde{y}|m) dt \tag{11}$$

$$\leq \int \left(-\ln p(\tilde{y}|m) + D_{\mathrm{KL}}(q(\vartheta)||p(\vartheta|\tilde{y}, m))\right) dt \tag{12}$$

$$= \int \left(\langle -\ln p(\tilde{y}, \vartheta|m)\rangle_q - \langle -\ln q(\vartheta)\rangle_q\right) dt, \tag{13}$$

where ϑ is internal parameter including causes $\tilde{x}$ and $\tilde{v}$. Distribution q is (arbitrary) recognition density. Here, we define the free-energy $\mathcal{F}$ as

$$\mathcal{F} := -\ln p(\tilde{y}|m) + D_{\mathrm{KL}}(q(\vartheta)||p(\vartheta|\tilde{y}, m)) \tag{14}$$

$$= \langle -\ln p(\tilde{y}, \vartheta|m)\rangle_q - \langle -\ln q(\vartheta)\rangle_q. \tag{15}$$

The free-energy is an upper bound of sensory entropy. The free-energy principle says that recognition is realized by minimizing this free-energy.

Here, we assume that the recognition density $q(\tilde{x}, \tilde{v})$ can be factorized into $q(\tilde{x})$ and $q(\tilde{v})$ (mean field approximation), and has a Gaussian form with means $\tilde{\mu}_x$ and $\tilde{\mu}_v$ (Laplace assumption). We also assume that noise $\tilde{z}_v$ obeys $\mathcal{N}(0, \Sigma_v)$, where $\tilde{\mu}_v = \tilde{v}_{\mathrm{pr}} + \tilde{z}_v$. Then, the free-energy can be written by (ignoring constant)

$$\mathcal{F} = \frac{1}{2}\varepsilon_y^T \mathit{\Pi}_y \varepsilon_y + \frac{1}{2}\varepsilon_x^T \mathit{\Pi}_x \varepsilon_x + \frac{1}{2}\varepsilon_v^T \mathit{\Pi}_v \varepsilon_v - \frac{1}{2}\ln|\mathit{\Pi}_y| - \frac{1}{2}\ln|\mathit{\Pi}_x| - \frac{1}{2}\ln|\mathit{\Pi}_v|, \tag{16}$$

$$\varepsilon_y = \tilde{y} - \tilde{C}\tilde{\mu}_x, \tag{17}$$

$$\varepsilon_x = D\tilde{\mu}_x - \tilde{A}\tilde{\mu}_x - \tilde{B}\tilde{\mu}_v, \tag{18}$$

$$\varepsilon_v = \tilde{\mu}_v - \tilde{v}_{\mathrm{pr}}, \tag{19}$$

where precision matrices $\mathit{\Pi}_y, \mathit{\Pi}_x$, and $\mathit{\Pi}_v$ are defined as the inverse of covariance matrices Σ_y, Σ_x, and Σ_v.

Thus, we can obtain the inversion (perception) model by gradient descent of minimizing free-energy as follows

$$\dot{\tilde{\mu}}_x = D\tilde{\mu}_x - k_1(-\tilde{C}\mathit{\Pi}_y\varepsilon_y + (D - \tilde{A})\mathit{\Pi}_x\varepsilon_x), \tag{20}$$

$$\dot{\tilde{\mu}}_v = D\tilde{\mu}_v - k_1(-\tilde{B}\mathit{\Pi}_x\varepsilon_x + \mathit{\Pi}_v\varepsilon_v). \tag{21}$$

Note that $\tilde{\mu}_x$ and $\tilde{\mu}_v$ are estimated values of $\tilde{x}$ and $\tilde{v}$.

One of the advantages of this perception model is that the equations (20) and (21) reflect cortical circuitry as shown in Fig. 1. It consists of thalamus, lower cortex, and higher cortex. Sensory input enters from environment through thalamus to the lower cortex, while prior knowledge enters from the higher cortex to the lower cortex. The cortical circuit estimates states in deep layers and conveys estimation to the lower area, while it also calculates estimation errors in superficial layers and conveys errors to the higher area.

3 MODELING OF ACETYLCHOLINE

In this section, we introduce ACh effects in the above perception model proposed by Friston [1]. Then, ACh dynamics is derived by the free-energy principle.

3.1 Introduction of acetylcholine effects

Yu and Dayan have proposed ACh model in a framework of hidden Markov model, suggesting that ACh represents uncertainty of top-down information, and controls the balance between bottom-up and top-down input [6], [7]. So, we also start with the following assumption.

Assumption: Let α denote the ACh level. Then, ACh controls the magnitude of top-down input as follows

$$\mathit{\Pi}_v = \pi_v \exp(-\lambda_v \alpha), \tag{22}$$

where π_v is prior precision matrix, and λ_v is positive constant.

The high ACh level decreases the magnitude of precision matrix $\mathit{\Pi}_v$, resulting in decreasing the contribution of ε_v to estimation in (21). In other words, ACh suppresses top-down processing. It corresponds to muscarinic feedback suppression by ACh released from the basal forebrain as shown in Fig. 1.

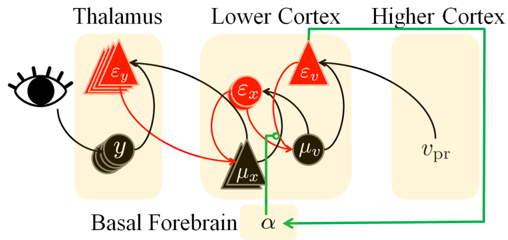

Fig. 1. Neuronal implementation of perception model with cholinergic modulation

3.2 Derivation of acetylcholine dynamics

Since we defined cholinergic modulation, we next derive dynamics of ACh level by the free-energy principle. Assuming that α obeys prior distribution $\mathcal{N}(\alpha_{\rm pr}, \varPi_\alpha)$, the free-energy is given by

$$\begin{aligned}\mathcal{F} = &\frac{1}{2}\varepsilon_y^T \varPi_y \varepsilon_y + \frac{1}{2}\varepsilon_x^T \varPi_x \varepsilon_x + \frac{1}{2}\varepsilon_v^T \pi_v \varepsilon_v \exp(-\lambda_v \alpha)\\ &-\frac{1}{2}\ln|\varPi_y| - \frac{1}{2}\ln|\varPi_x| - \frac{1}{2}\ln|\pi_v| + \frac{1}{2}\lambda_v \alpha\\ &+\frac{1}{2}\varepsilon_\alpha^T \varPi_\alpha \varepsilon_\alpha - \frac{1}{2}\ln|\varPi_\alpha|,\end{aligned} \quad (23)$$

where $\varepsilon_\alpha = \alpha - \alpha_{pr}$. Because the ACh level changes slower than state estimation, ACh minimizes the time integral of the free-energy by gradient descent as follows

$$\dot{\alpha} = -k_2 \partial_\alpha \int \mathcal{F} dt \quad (24)$$

$$= -k_2 \int (\frac{1}{2}\lambda_v - \frac{1}{2}\lambda_v \varepsilon_v^T \pi_v \varepsilon_v \exp(-\lambda_v \alpha) + \varPi_\alpha \varepsilon_\alpha) dt. \quad (25)$$

By time differentiating of both sides, we obtain ACh dynamics.

Derived dynamics: ACh level changes according to

$$\ddot{\alpha} = -k_2(\frac{1}{2}\lambda_v - \frac{1}{2}\lambda_v \varepsilon_v^T \pi_v \varepsilon_v \exp(-\lambda_v \alpha) + \varPi_\alpha \varepsilon_\alpha). \quad (26)$$

Instead of using gradient descent, the optimal ACh level that minimizes the free-energy at each time can be written analytically by solving $\partial_\alpha \mathcal{F} = 0$ and assuming that $\varPi_\alpha$ is close to zero. The optimal ACh level can be written by

$$\alpha = \frac{1}{\lambda_v} \ln \varepsilon_v \pi_v \varepsilon_v. \quad (27)$$

This equation shows that the ACh level varies proportional to the square of the estimation error ε_v. In other words, the ACh level represents the magnitude of estimation errors associated with top-down information in perception. Released ACh affects the efficacy of top-down modulation.

4 SIMULATION

We first simulate the generative model to create observed data, and then simulate the perception model with cholinergic modulation using sensory data given by the generative model. We use time step $\Delta t = 0.01$ in both the generative and perception model.

4.1 Generative model

In our simulation, the generative model creates 2 dimensional state x and 4 dimensional output y according to the equations (3) and (4) with scholar input v, given by

$$\begin{aligned}v(t) = &\tanh(t-70) - \tanh(t-130)\\ &+\tanh(t-270) - \tanh(t-330)\\ &+\tanh(t-470) - \tanh(t-530) + z_v.\end{aligned} \quad (28)$$

Embedded order of generalized coordinates is $n = 3$. We used the following constant parameters

$$A = \begin{bmatrix}-0.25 & 1.00\\ -0.50 & -0.25\end{bmatrix}, B = \begin{bmatrix}1\\0\end{bmatrix},$$
$$C = \begin{bmatrix}0.1250 & 0.1633\\ 0.1250 & 0.0676\\ 0.1250 & -0.0676\\ 0.1250 & -0.1633\end{bmatrix}, \quad (29)$$

and precision matrices

$$\begin{aligned}\varPi_y &= S \otimes I_4 \exp(10),\\ \varPi_x &= S \otimes I_2 \exp(4),\\ \varPi_v &= S \exp(6),\\ S &= \begin{bmatrix}1 & 0 & -\frac{1}{2}\gamma & \cdots\\ 0 & \frac{1}{2}\gamma & 0 & \\ -\frac{1}{2}\gamma & 0 & \frac{3}{4}\gamma^2 & \\ \vdots & & & \ddots\end{bmatrix}^{-1},\end{aligned} \quad (30)$$

with a roughness parameter $\gamma = 4$. These parameterizations are similar to [1].

Simulation results of the generative model are shown in Fig. 2. Input v becomes high at time t = 70∼130, 270∼330, and 470∼530. State x and output y vary depending on the input v. In our simulation, we raise the noise level to $\varPi_y = S \otimes I_4 \exp(8)$ at time t = 200∼400.

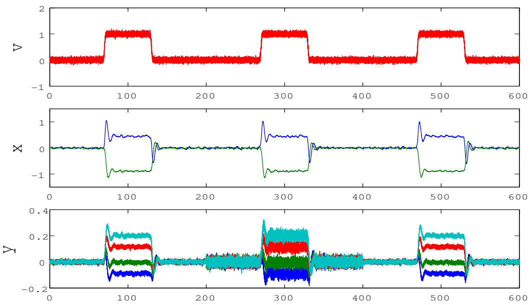

Fig. 2. Generative model

4.2 Perception model with cholinergic modulation

Next, we simulate the perception model (20) and (21) with ACh effects (22) and (26). We used parameters

$$\varPi_\alpha = 1, \alpha_{pr} = 0, \quad (31)$$
$$\pi_v = S \exp(6). \quad (32)$$

A, B, C, Π_y, and Π_x are the same as those of the generative model. Afferent input y is noisy at time $t = 200 \sim 400$, while prior knowledge v_{pr} is noisy at time $t = 400 \sim 600$.

Simulation results are shown in Fig. 3. Cortical circuitry estimates states μ_x and μ_v, changing the ACh level α in response to estimation errors at the same time. Estimated states μ_x and μ_v are similar to true dynamics in the generative model in Fig. 2. The ACh level α has oscillatory behavior after afferent input comes in. When prior knowledge is noisy, the ACh level becomes high. This means that ACh reports uncertainty of top-down information. The lower two figures show the free-energy $\mathcal{F}$ in the case of proper cholinergic modulation (above) and cholinergic deficit in which α is always zero (bottom). Although the free-energy level increases when afferent input as well as prior knowledge is noisy regardless of cholinergic modulation, ACh suppresses the rise of the free-energy in the case of noisy prior knowledge. As a result, ACh yields better perception.

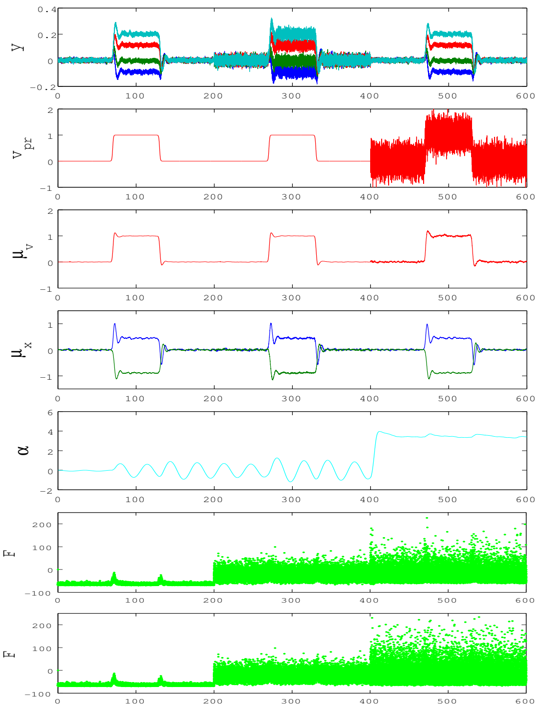

Fig. 3. Perception model with cholinergic modulation (above) and without cholinergic modulation (the lowest)

5 DISCUSSION

The role of ACh in this study is similar to that of [6] and [7], which is based on hidden Markov model, because both suggest that ACh reports uncertainty associated with top-down information. The biggest difference is that ACh contributes to efficient calculation in [6] and [7], whereas it contributes to estimation precision in our model, which is thought to be more realistic.

In addition to changing the ACh level depending on the noise level, ACh has oscillatory behavior. This is because the ACh level is defined by the "time integral" of the free-energy and thus its dynamics is written by quadratic differential equation. This fact indicates the possibility that oscillations in the brain can occur by minimizing the time integral of the free-energy.

Besides inserting cholinergic modulation effects in Σ_v, we can also introduce ACh effects in Σ_y and Σ_x [5]. These effects correspond to nicotinic thalamo-cortical facilitation and muscarinic intracortical suppression [3], [4]. We consider that the effects on Σ_v, Σ_y, and Σ_x result in noise reduction of prior knowledge, noise reduction of afferent input, and detection of mismatch of prior knowledge and afferent input, respectively.

6 CONCLUSION

In this paper, we introduce cholinergic modulation effects in a perception model based on the free-energy principle. The effects correspond to muscarinic top-down suppression. Then, we derive ACh dynamics by the free-energy principle. Our model suggests that the ACh level increases when top-down input is noisy, that is, ACh represents uncertainty of top-down information. Precise perception can be realized by cholinergic top-down modulation.

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REFERENCES

[1] Friston K (2008), Hierarchical models in the brain. PLoS Comput Biol 4(11):e1000211

[2] Friston K (2010), The free-energy principle: a unified brain theory? Nat Rev Neurosci 11: 127–138

[3] Gil Z, Connors BW, Amitai Y (1997), Differential regulation of neocortical synapses by neuromodulators and activity. 19(3):679–686

[4] Hasselmo ME (2006), The role of acetylcholine in learning and memory. Current Opinion in Neurobiology 16(6):710–715

[5] Takada M, Aihara K (2012), A mathematical model of cholinergic function based on the free-energy principle. Cosyne Abstracts, Salt Lake City USA (submitted).

[6] Yu AJ, Dayan P (2002), Acetylcholine in cortical inference. Neural Networks 15:719–730

[7] Yu AJ, Dayan P (2005), Uncertainty, neuromodulation, and attention. Neuron 46:681–692