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Motor control: Neural correlates of optimal feedback control theory

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Recent work is revealing neural correlates of a leading theory of motor control. By linking an elegant series of behavioral experiments with neural inactivation in macaques with computational models, a new study shows that premotor and parietal areas can be mapped onto a model for optimal feedback control.

We are constantly adapting. Whether it is to new shoes, or walking on icy terrain, we have the capacity to continually update our motor actions in a goal-directed manner. The leading theory of how we do this — optimal feedback control (OFC) theory — has been upheld by an impressive number of elegant behavioral studies in humans and other animals over the last 20 years, yet the neural circuits that implement such control continue to remain elusive. Now, in a study reported in this issue of *Current Biology*, Takei *et al.*[1] have chipped away at this long-standing question in motor control by providing important clues to how neural circuits may begin to be mapped onto theory.

The origins of optimal control date back nearly 300 years, but in the 1950s Wiener's cybernetics movement brought forth the notion that intelligent behavior is rooted in feedback control. OFC theory burst onto the motor control scene in 2002 with seminal work by Todorov and Jordan[2]. They postulated that, by deploying stochastic optimal feedback control, the motor system would only correct movements in task-relevant dimensions. This allows variability in task-irrelevant ones, and this 'minimum intervention' principle nicely explains many motor behaviors of humans.

The model was a breakthrough in several respects. Firstly, this framework requires multiple parts: an internal forward model that enables the computation of optimal control signals (given noisy, delayed feedback), which is integrated with knowledge of the body dynamics and the available copy of the out-going motor command (the so-called efference copy; Figure 1A) via a state-estimator. Secondly, the goal-directed nature of the motor corrections beautifully matched many observations. The model is allowed to exploit redundancy to improve performance, which matches to observations of motor variability, and task-relevant motor corrections that occur mostly closest to the end-goal (for example, correcting hand movements mid-trajectory to match an average trajectory template is not required; what is required is hitting the end-goal). Lastly, in contrast to other theories of motor control, such as active inference[3] or feedback error learning[4], OFC theory does not require a trajectory template and explicitly considers noise and delays, which are important constraints of biological systems.

Shortly thereafter, Scott[5] hypothesized that, because OFC theory was so powerful at explaining human movement and consists of multiple elements, it could be highly valuable for mapping the neural basis of goal-directed (volitional) motor control. He laid out several crucial neural observations that matched with OFC theory. For example, the observed tuning-properties of motor cortex (M1) neurons activity were found to change in a behaviorally dependent manner. This powerful idea has spawned years of research into how the observed behaviors of the motor system — which without a doubt must include such notions as internal forward models and goal-directed corrections — can be mapped onto neural circuits.

Techniques such as optogenetics or chemogenetics allow experimentalists to design studies where one can spatially (in the brain) and temporally (in the behavioral space) perturb neural circuits during motor behaviors[6–9]. While this is mostly limited to rodent studies, the future holds these types of experiments in non-human primates. In their new work, Takei *et al.*[1] have causally tested OFC theory in a non-human primate species with an elegant use of cooling probes in multiple areas of the macaque cortex[1,10].

In prior work, Scott and colleagues[11] showed that many regions of cortex respond rapidly to limb perturbations. Specifically, they recorded in five cortical regions that are involved in motor control: parietal area 5 (A5), primary somatosensory cortex areas 1 and 2 (S1, S2), M1, and dorsal premotor cortex (PMd)). They found that the delays of sensory information from the periphery could change in a task-relevant manner. Namely, if limb-perturbations were important for the ongoing task, the measured response times in A5, S1 were only ~25 milliseconds, yet a target-selection change first causes responses in PMd and M1 (with other regions trailing behind). This was intriguing evidence that parietal areas, such as A5, might play a crucial role in task-relevant corretions.

Building on their earlier work[5,11,12], Takei *et al.*[1] have now causally tested the role of A5 and PMd during limb perturbations applied during a postural stabilization task. First, they mapped their behavioral paradigm onto the OFC theory model and performed a series of 'inactivation' experiments to investigate what model parameters have differential effects on the predicted behavior. The model has several key parameters that they test: the 'Kalman gain' (**K**), which is the term that provides an uncertainty measure (that modulates the learning rate); the internal forward model

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observation ($\hat{\mathbf{H}}$); and the 'feedback' (**L**) from the 'state estimator' (the estimated state of the body) to the controller (the region that sends out motor commands). Formally, Takei *et al.* test variations of all three components — the internal forward model, state estimator and feedback control policy — of an OFC model. The true system state **x** is transformed into measurements (observations) **y** by means of an observation matrix **H** and passed to the state estimator. Based on the measurement noise, the state estimator trades off these measurements with a current state estimate, controlled by the Kalman gain **K** (Figure 1A). The state estimator computes the difference of the actual vs. expected sensory feedback by transforming the output of the internal forward model by an observation matrix $\hat{\mathbf{H}}$**.** The state estimation result is finally fed back into the control policy, where it is scaled with the feedback gain **L** (Figure 1A). Modifying the aforementioned parameters can non-trivially affect the system behavior. The results of this parameter testing are summarized in Figure 1B; namely, if they inactivate '**L**' they predict a change in response speed, and if a strong reduction in **L**, or in **H**, there is also an endpoint error. In contrast, if **L** is normal, but **K** is modified, they predict an endpoint error, but no response-speed changes.

Next, in an elegant series of experiments in which cooling probes were used to inactivate spatial regions of the macaque brain[10,13], Takei *et al.*[1] found differential effects by cooling A5 and PMd, suggesting they may play different roles that can be mapped to OFC theory. Cooling only A5 increased endpoint error, while inhibition of PMd both increased endpoint error and reduced the response accuracy, among other metrics. While the former finding directly links to the effect of downscaling the Kalman gain in an OFC theory model — highlighting that A5 cooling impairs state estimation — both reduction of sensory input and the feedback control gain in OFC theory qualitatively predict the effect of cooling PMd (Figure 1). In a series of additional experiments combining cooling of both PMd and A5, the authors went on to show that impairments in endpoint errors and response speed add up linearly and scale sublinear for the maximally observed deviation. They found that only

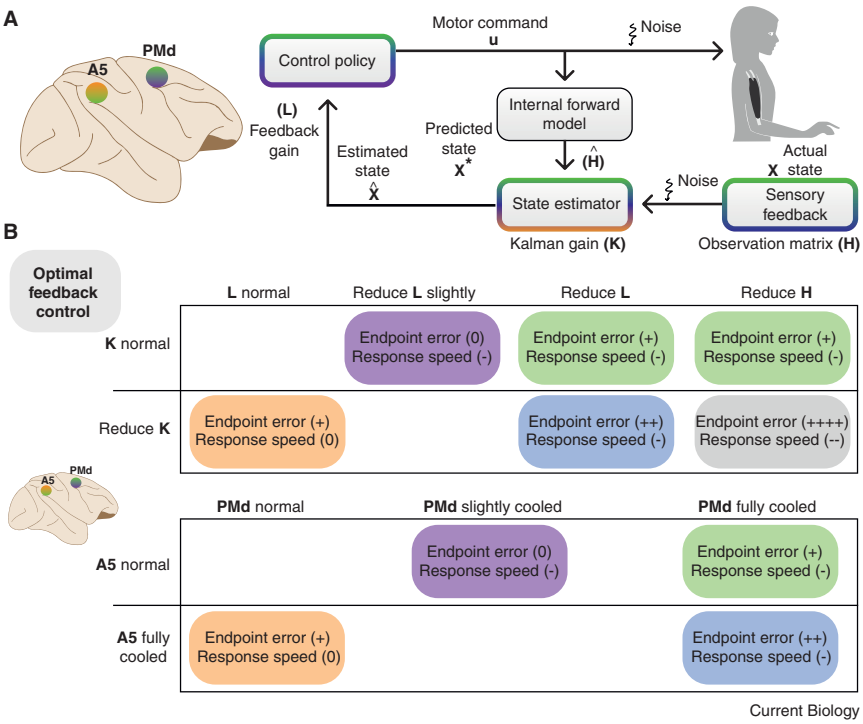

Figure 1. OFC theory and the brain.
(A) Highlights optimal feedback control theory, the brain regions perturbed, and the colors highlight the matching model-to-brain predictions. '**L**' is the feedback gain, '**K**' is the Kalman gain in the state estimator, '**H**' is the observation matrix modeling the measurement of the actual state **x**, while **H** transforms the corresponding estimated states **x*** the state estimator receives from the forward model. Other terms are defined on the figure, but not directly tested in the author's report. (B) The main results from both the modelling work and the experimental testing are summarized. Note, the paired colors highlight where the model matched. The (0) means no change predicted/observed; (+) means increased, (–) means decreased behavioral changes. During combinations of cooling experiments, these changes can add up (thereby increasing the number of + or – displayed in the table). (Cartoon images are by Smith Breault, Macauley (CC 4.0) from scidraw.io.)

simultaneous attenuation of the Kalman gain and the feedback control gains in OFC theory, but not attenuation of Kalman gain and sensory input, could reproduce these observations in the model (Figure 1B, grey box prediction).

Adding to this evidence of a link between PMd cooling and reduction of the feedback control gain, Takei *et al.*[1] consider partial cooling of PMd as a third paradigm and model this as a smaller reduction in the feedback gain. The model yields a characteristic response in this setting: in contrast to the full reduction experiment, partial impairment no longer impacts the endpoint error (previously, an increase was observed in all of the A5, PMd and A5 plus PMd cooling experiments). Alternatively to reducing parameters in the OFC theory model, single impairments of PMd or A5 can also be modeled by increasing the noise levels on the feedback or Kalman gain parameters, respectively. However, the results of the partial cooling experiment could be solely explained by downscaling the feedback gain.

Overall, Takei *et al.*[1] build on previous findings regarding the role of A5 and PMd in motor control by mapping their role to specific parameters in optimal feedback control theory. Specifically, the model predictions matched the experimental predictions in several key domains. As we summarize in Figure 1B, parameters involved in both control policy (L), and the state estimator (K, H), could be mapped to PMd and A5, respectively.

In the future, it will be important to address some limitations of this work, and build on it in new ways. While Takei *et al.*[1] demonstrate links between OFC theory predictions, A5, PMd and behavior, it is likely that the model can be enriched by taking into account the circuits themselves. Fundamentally, OFC theory

is a phenomenological model, and how neurons implement its components such as the Kalman gain is unresolved. Moreover, there are numerous potential implementations at the circuit level, such that new models that provide concrete experimental hypotheses will be important.

To work in this direction, more fine-grained cooling experiments might yield richer input to the model (and, of course, more temporally and cell-type-specific approaches such as optogenetics will become important). The same applies for deactivating additional individual brain regions. These additional choices for influencing the biological brain will apply to identify interesting working points of the OFC theory model with unique response patterns. Reproducing such patterns in the biological system and adding them in the author's combinatorial experimental design (Figure 1B) will shed even more light on links between biological brains and OFC theory model components, and indicate where more complex models are needed for an accurate account of the neural implementation[14,15].

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