

levels of polymorphism and play a role in individual recognition in other species with similar demographic and behavioural features to those of the house mouse.

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Optimal Control: When Redundancy Matters

A new experiment provides support for optimal feedback control as a theoretical basis of how the motor system responds to perturbations in a context-dependent manner.

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In motor control, two striking features set the human body apart from its robotic counterparts. First, the human musculoskeletal system has a tremendous amount of redundancy. For example, if we consider the arm, there are multiple muscles controlling each joint and many more degrees of freedom in the skeletal structure than are needed to specify the position and orientation of the hand. Second, the amount of trial-by-trial variability in the output of the muscles is considerable compared to typical torque motors used in robotic applications. Nevertheless humans show dexterity that currently outperforms any robot. A recent theory of biological motor

control has suggested that redundancy and variability go hand-in-hand, in that redundancy allows the body to compensate efficiently for errors that arise during movement [1,2].

The theory is known as stochastic optimal feedback control, and has been applied to explain a wide range of motor behaviours [3–6]. The mathematics of optimal control was largely developed in the 1950s by Bellman [7] in the United States and Pontryagin [8] in Russia. The theory addresses a fundamental problem: given an object under our control, such as an arm, and a performance criterion (usually specified as a cost function that can depend on variables such as energy or accuracy), what is the best action that can be performed — that

is, the one that minimizes the cost.

One of the most important contributions of stochastic optimal control theory to the field of biological motor control is that it not only explains average movement trajectories repeated over many trials, but also trial-by-trial variability. This variability sets us apart from robots that usually replicate the very same stereotypical movements with high precision on large production lines. In contrast, we never make exactly the same movement twice even for the same task. The theory of optimal feedback control explains how the motor system can exploit the properties of the human body. Key to this theory is the concept of task-irrelevant dimensions — combinations of control parameters which can be altered without affecting task achievement. For example, if you want to hold your hand at a location in space, changes in the set of shoulder, wrist and elbow joint angles that do not change the position of your hand can be regarded as a task-irrelevant

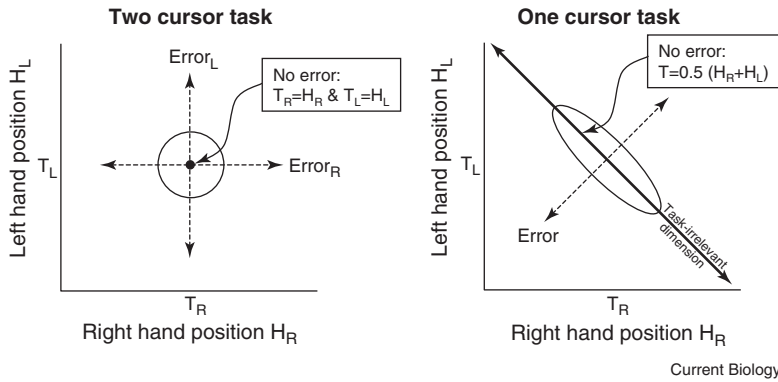


Figure 1. Exploitation of redundancy by an optimal controller.

When each hand controls a separate cursor (left), both cursors are controlled independently to their respective targets (T_R and T_L). Therefore, there is only one setting of hand positions for which there is no error. There is no correlation between the endpoint positions (black circle shows a schematic distribution of errors). When the two hands control the position of one cursor to a single target T (right) there are many combinations of final hand positions which give zero error (black diagonal line). This is the task-irrelevant dimension in that any variation in this direction does not affect the error as it corresponds to moving the hands either apart or together which does not change the cursor position which is the average of the two hands locations. Optimal control predicts negative correlations between the final locations of the two hands, so that if one hand is too far to the left the other compensates by moving to the right (black ellipse). Adapted from [1].

change. Allowing fluctuations in such task-irrelevant dimensions is the optimal strategy because control can be focussed on task-relevant dimensions. This is called the minimum intervention principle, as you avoid making any corrections to perturbations that do not interfere with task goals [2].

As reported recently in *Current Biology*, on the basis of this principle Diedrichsen [9] developed a paradigm to experimentally test this theory. In his experiment, subjects were exposed to two different tasks in which they made bimanual reaching movements in a virtual reality system. In the first task, each hand controlled a cursor and each cursor had to be moved to its respective target. This required subjects to place their left hand position, H_L , and their right hand position, H_R , on separate targets. In a second task, subjects controlled a single cursor, the position of which was located at the point mid-way between the two unseen hands: $1/2 (H_L + H_R)$. This way an artificial redundancy was created in the control task.

What are the predictions for control in these tasks within the optimal control theory framework? In the two cursor task there is no task-irrelevant dimension, as each hand has to be placed on its target,

and as expected there was no correlation between the errors that each hand made (Figure 1A). However, by introducing the new redundancy, the number of task-relevant variables, that is the single cursor position, is lower than the total number of control variables (the two hand positions). Therefore, there are combinations of control variables that do not affect the task variable. Provided the average location of the hands is on target, the actual final locations of each hand can vary along the task-irrelevant direction (Figure 1B). This predicts that there should be a negative correlation between the final locations of the two hands — which is exactly what Diedrichsen [9] found experimentally.

Moreover, one of the subject's hands could be perturbed by a robotic interface during the movement. As expected, when each hand controlled its own cursor, the perturbed hand would rapidly correct, and the other hand showed no reaction to the perturbation. When the two hands controlled a single cursor and one of the hands was perturbed, its response was smaller than in the two cursor task. Importantly, even though there was no mechanical coupling between the hands, the

other, unperturbed hand now made a corrective movement. This is precisely what optimal feedback control predicts, as now the other hand contributes to the task-relevant parameter. Importantly, when perturbations were introduced in the absence of visual feedback, subjects showed a behavioural response appropriate for each task. Without visual feedback, the two cursor and the one cursor tasks have identical sensory inputs. This suggests that subjects can set up different feedback controllers based solely on task requirements.

This explanation is of particular interest as the task dependency of behavioural changes cannot easily be explained by previous theories of motor control. One of the most popular traditional concepts is the desired trajectory hypothesis [10,11]. In this framework, movement execution consists in tracking pre-computed desired trajectories, which is in stark contrast to optimal feedback control theories, where the trajectory is an emergent phenomenon generated on-line. In such a framework the task goals would be defined in terms of desired trajectories of the cursors and this would be used to specify the two desired hand trajectories. If one hand is then perturbed there is no need for the other hand to correct since it still follows its desired trajectory. So the desired trajectory hypothesis fails to explain the change in behaviour.

A similar line of argument can be applied with regard to another motor control theory: the equilibrium point hypothesis [12,13]. The basic idea of this theory is that the control system exploits the muscle's spring like properties by controlling the equilibrium posture of the arm. Movements are made by changing the equilibrium posture. For both tasks, however, the equilibrium points for the two arms would be specified independently. Consequently, any perturbation applied to only one of the arms would result in a unimanual response to the disruption towards the specified equilibrium point. Again this does not explain the data.

The new study by Diedrichsen [9] provides a direct test of optimal feedback control by means of a simple and elegant experiment. It shows how task-dependent changes in bimanual coordination can be explained within the framework of optimal feedback control, while previous theories of motor control cannot account for the experimental findings. The next step is to gain a deeper theoretical understanding of the adaptive processes that occur during learning of novel dynamics.

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Developmental Biology: Micro(RNA)-Managing Nodal

Nodal signaling plays an essential role during the induction and patterning of vertebrate embryonic tissue types. In *Xenopus* and zebrafish, microRNAs regulate Nodal signaling, but surprisingly by very different mechanisms.

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The establishment of the vertebrate body plan is a complex process requiring the precise control of induction, patterning and morphogenesis. The growth factors that coordinate these events must be tightly regulated, ensuring the correct dose of growth factor at a particular time and place for proper embryogenesis to occur. This has become increasingly evident with the recent discoveries that microRNA (miRNA) regulation of Nodal pathway members is required for the proper development of frog and fish embryos [1,2]. These studies represent the first examples of developmental growth factor regulation by miRNAs.

Formation of the vertebrate body relies on conserved principles of development [3]. All vertebrates create three primary germ layers:

the endoderm, the mesoderm and the ectoderm. The organizer, which will later become the head, patterns the germ layers, with tissues closer to the organizer adopting a dorsal fate and more distant tissues a ventral one (Figure 1A) [4–6]. Fundamental to the process of germ layer induction and patterning is the Nodal signaling pathway, which is essential for proper endoderm and mesoderm formation [5–7].

The Nodals are members of the transforming growth factor- β family of secreted ligands, which signal through type I and type II serine-threonine kinase receptors (Figure 1B). Proper Nodal signaling also requires the EGF-CFC family of co-receptors, which bind directly to the type I receptor. Nodals are antagonized by secreted Lefty proteins, which can bind directly to Nodals and the EGF-CFC co-receptor to block signaling [8].

Despite the conserved role of Nodal signaling as a major player

in early vertebrate development, clear differences exist between species in their specific use of the Nodal ligands. For example, *Xenopus* have five Nodals that are expressed early during development [9], two of which exhibit very early asymmetric expression across the dorsal-ventral axis [10], while zebrafish only have two Nodals expressed early, one of which has a very brief asymmetric expression [11]. And while Nodals are clearly required for endoderm and mesoderm induction in both species, their roles in patterning outside of the organizer may differ between fish and frogs [5]. It seems fitting, then, that miRNAs regulate the Nodal pathway in both *Xenopus* and zebrafish, but appear to do so by targeting different members of the signal transduction pathway with separate developmental outcomes.

Recently, miRNAs have emerged as major players in the control of gene expression [12]. miRNAs begin their life as primary RNAs that are processed by the RNase III endonucleases Droscha and Dicer into ~22 base noncoding RNAs, which are complementary to sequences within the 3' untranslated region (UTR) of target mRNAs [13]. When bound to their targets, miRNAs can promote mRNA cleavage or deadenylation