cleaves the Rec8 component of cohesin. However, it is important to note that there may be more to it than this. In budding yeast, separase activation promotes an increase in its kinesin-5 motor protein Cin8 [10], and the experimental design adopted by the FitzHarris study does not rule out such a signaling process also being involved in mouse eggs.

The conclusion that ip-MT-based sliding movement may initially underlie chromosome segregation agrees with previous observations that kinetochores are not required for anaphase movement in mouse eggs [11]. Here DNA beads introduced into eggs by microinjection undergo anaphase poleward movement with similar timing to sister chromatids despite their lack of kinetochores. It is also interesting that *Caenorhabditis elegans* oocytes also appear to have developed a kinetochore-free method of pushing chromosomes apart in the two meiotic divisions that follow their fertilization [12]. Here kinetochores are dispensed with for all of anaphase and instead chromosomes are segregated by pushing forces emanating from the spindle mid-zone.

In the mouse egg the kinesin-5-driven spindle elongation emanating from ip-MT sliding is then followed by Anaphase A. Using a photoactivatable form of tubulin to draw by laser a line across the spindle microtubules and perpendicular to the axis of the spindle, it was shown that the majority of the pole–kinetochore shortening was achieved by destabilization of k-MTs at their kinetochores. Anaphase A is described to occur by so-called Pacman-flux: Pacman-driven k-MT shortening at the kinetochore combined with microtubule loss at the poles [13]. Future studies are therefore needed to understand which factors are involved in this Pacman-flux in mouse eggs.

The need to segregate sister chromatids initially through spindle lengthening may seem odd in a cell that already possesses a large spindle at metaphase: $\sim$25 μm pole-to-pole in length in a cell that is 70 μm in diameter. However, peculiar to rodent eggs is the orientation of the meiotic spindle, with the axis of the spindle running tangential to the plasma membrane. The spindle is anchored in this tangential position to the cortex by nucleation of F-actin, which is maintained by activation of the Arp2/3 complex [14]. During egg activation, spindle rotation is needed to produce the second polar body, but this rotation event follows, rather than precedes, anaphase [15]. As such, the initial rapid lengthening of the meiotic spindle and associated separation of sister chromatids in Anaphase B of mouse eggs may be the most effective route for extruding a polar body with a minimum amount of cytoplasmic loss. By ‘effective’, it is meant that the actual increase in the spindle length at this time may push both spindle poles against the plasma membrane, and this surface contact then triggers the process of rotation and cytokinesis. In the absence of such spindle lengthening this contact may be delayed or not be close enough to trigger abcission, or would have to pinch off more cytoplasm into the polar body. If the unusual orientation is at all behind the timing of Anaphase A and B in mouse eggs, then it would be worthwhile replicating the experiments performed by FitzHarris in eggs such as those of monkey or human, where the axis of the spindle is perpendicular to the plasma membrane, and no spindle rotation is needed for polar body extrusion [16]. It remains possible that rodent eggs have adopted this method of Anaphase as a consequence of the unusual orientation of their spindle.

References

1. Peters, J.M. (2006). The anaphase promoting complex/cyclosome: a machine designed to destroy. Nat. Rev. Mol. Cell Biol. *7*, 644–656.
2. Musacchio, A., and Salmon, E.D. (2007). The spindle-assembly checkpoint in space and time. Nat. Rev. Mol. Cell Biol. *8*, 379–393.
3. FitzHarris, G. (2012). Anaphase B precedes Anaphase A in the mouse egg. Curr. Biol. *22*, 437–444.
4. Brust-Mascher, I., and Scholey, J.M. (2011). Mitotic motors and chromosome segregation: the mechanism of anaphase B. Biochem. Soc. Trans. *39*, 1149–1153.
5. Jones, K.T. (2005). Mammalian egg activation: from Ca2+ spiking to cell cycle progression. Reproduction *130*, 813–823.
6. Madgwick, S., Hansen, D.V., Levasseur, M., Jackson, P.K., and Jones, K.T. (2006). Mouse Emi2 is required to enter meiosis II by reestablishing cyclin B1 during interkinesis. J. Cell Biol. *174*, 791–801.
7. Shoji, S., Yoshida, N., Amanai, M., Ohgishi, M., Fukui, T., Fujimoto, S., Nakano, Y., Kajikawa, E., and Perry, A.C. (2006). Mammalian Emi2 mediates cytostatic arrest and transduces the signal for meiotic exit via Cdc20. EMBO J. *25*, 834–845.
8. Ferenz, N.P., Gable, A., and Wadsworth, P. (2010). Mitotic functions of kinesin-5. Semin. Cell Dev. Biol. *21*, 255–259.
9. Tachibana-Konwalski, K., Godwin, J., van der Weyden, L., Champion, L., Kudo, N.R., Adams, D.J., and Nasmyth, K. (2010). Rec8-containing cohesin maintains bivalents without turnover during the growing phase of mouse oocytes. Genes Dev. *24*, 2505–2516.
10. Khmelinskii, A., Roostalu, J., Roque, H., Antony, C., and Schiebel, E. (2009). Phosphorylation-dependent protein interactions at the spindle midzone mediate cell cycle regulation of spindle elongation. Dev. Cell *17*, 244–256.
11. Deng, M., Gao, J., Suraneni, P., and Li, R. (2009). Kinetochore-independent chromosome poleward movement during anaphase of meiosis II in mouse eggs. PLoS One *4*, e5249.
12. Dumont, J., Oegema, K., and Desai, A. (2010). A kinetochore-independent mechanism drives anaphase chromosome separation during acentrosomal meiosis. Nat. Cell Biol. *12*, 894–901.
13. Zhang, D., Rogers, G.C., Buster, D.W., and Sharp, D.J. (2007). Three microtubule severing enzymes contribute to the “Pacman-flux” machinery that moves chromosomes. J. Cell Biol. *177*, 231–242.
14. Yi, K., Unruh, J.R., Deng, M., Slaughter, B.D., Rubinstein, B., and Li, R. (2011). Dynamic maintenance of asymmetric meiotic spindle position through Arp2/3-complex-driven cytoplasmic streaming in mouse oocytes. Nat. Cell Biol. *13*, 1252–1258.
15. Wang, Q., Racowsky, C., and Deng, M. (2011). Mechanism of the chromosome-induced polar body extrusion in mouse eggs. Cell Div. *6*, 17.
16. Brunet, S., and Verlhac, M.H. (2011). Positioning to get out of meiosis: the asymmetry of division. Hum. Reprod. Update *17*, 68–75.

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Motor Memory: When Plans Speak Louder Than Actions

A new study demonstrates that separate motor memories can be learned and remembered for two physically identical movements, provided that those movements have different goals.

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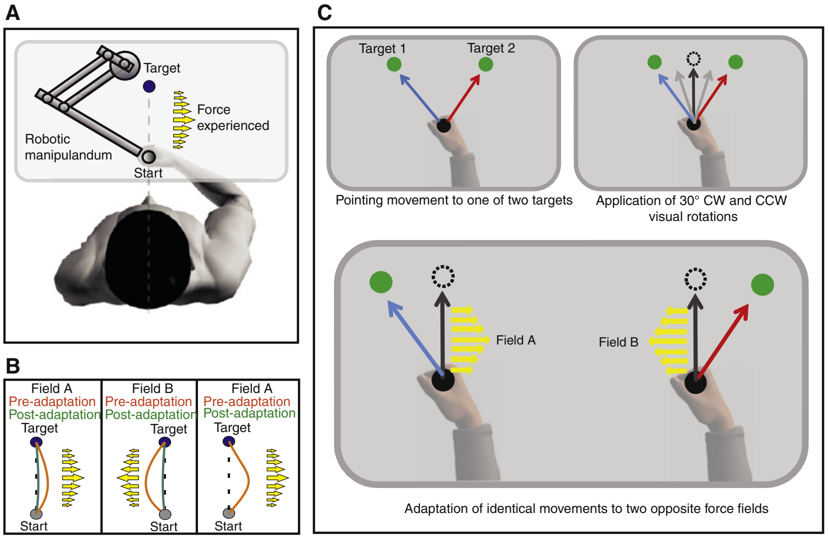
In our daily lives, we often encounter situations in which the relation between motor commands and their consequences is altered. For example, the mapping between arm motor commands and resultant arm motion changes when an object is grasped in



Current Biology

Figure 1. Experiments assessing multiple internal models.

(A) Example robotic manipulandum used to assess arm movement adaptation to a rotary viscous load that scales with hand velocity. Only the target and cursor remain visible to the participant. (B) Typical A – B – A motor learning paradigm. Participants perform succesive sets of reaching movements under opposing force fields (Field A and Field B). Initial training on Field A worsens performance on Field B, which in turn interferes with performance on Field A when experienced a second time. (C) Methods of Hirashima and Nozaki. Participants began reaching to two targets located either 30° clockwise (CW) or 30° counterclockwise (CCW). Gradual visual rotations in the same direction as the target were introduced, eventually allowing the same physical movement when participants were intending to move to two distinct visual targets. After the rotations were learned, opposing rotary viscous force fields were applied to each of the targets.

the hand. Moreover, this change will depend on the dynamics of the object, specifying the relation between applied force and motion. Many studies of motor learning have examined how people adapt their arm movements to perturbations that occur when moving a grasped object with novel dynamics, including rotary viscous loads (or force fields) that perturb the hand perpendicular to the direction of hand movement with a magnitude that scales with hand speed (Figure 1A). With practice, participants are able to gradually correct errors induced by the perturbation, indicating that they learn an internal model of the dynamics that captures the mapping between motor commands and consequences [1–5]. Despite this flexibility, such learning suffers a notable limitation — the motor system often has great difficulty learning more than a single internal model for any given set of movements at a single time [6–9]. For example, in a typical A – B – A paradigm where participants perform successive sets of similar reaching movements under opposing rotary viscous force fields (A and B) that perturb the arm in opposite directions, initial training on A worsens performance on B, which in turn worsens performance on A when A is experienced a second time (Figure 1B). In a series of experiments reported in this issue of *Current Biology*, Hirashima and Nozaki [10] provide behavioral evidence challenging the basic assumption that separate internal models cannot be learned and remembered for two physically identical movements.

The difficulty of learning more than a single internal model for a given set of movements can be accounted for quite well by state-space models of motor adaptation [11,12] in which internal model parameters are updated, trial-by-trial, based on movement errors. Specifically, if it is assumed that internal models of dynamics are learned in association with movement kinematics, such models predict that only a single internal model can be assigned to a given movement trajectory at a time [13]. Despite their predictive power, a number of studies have provided results that such state-space models have had difficulty explaining, at least without significant modification. For example, task savings observed in the relearning of a particular perturbation the second time it has been encountered are not predicted by basic single-timescale state-space models, yet are evident in behavior [14,15]. These findings suggest that at least certain parameters and/or assumptions of the model are not fully representative of how the brain solves perturbation problems.

In a clever series of experiments, the study by Hirashima and Nozaki [10] has provided behavioral evidence challenging the basic assumptions that only a single internal model can be assigned to a single set of movement kinematics. Participants repeatedly reached to two targets located 30° clockwise or counterclockwise from the straight ahead position. Concurrently, gradually increasing visual rotations of the on-screen cursor representing hand position were applied in the same direction as the target (Figure 1C). Ultimately, this allowed participants to perform physically identical pointing movements, even though participants were intending to move to two distinct visual targets and successfully moved the cursor to these targets. At this point, opposing rotary viscous force fields were applied to the two targets. The authors found that participants could readily adapt their movements to the two opposing fields presented in an interleaved design.

Hirashima and Nozaki [10] suggest that one possible way to reconcile these results with standard state-space models is by altering the way movements are represented in the brain. Rather than being represented in terms of actual movement kinematics, they suggest movements could be represented as a state of the sensorimotor transformation network used to map the visual target onto a motor command. This would allow distinct motor plans, associated with different visual targets, to be mapped onto distinct states of the neural network representing identical movement kinematics.

As discussed previously, the dominant account of state-dependent learning during motor adaptation assumes an iterative update of the internal model based on a combination of the errors experienced and the motor plans that resulted in those errors. However, in a recent paper Gonzales Castro and colleagues [16] challenge this assumption, suggesting instead that internal models are updated based on the errors experienced in combination with the actual motion states that led to those errors. The authors effectively demonstrate in their paradigm that the patterns of generalization associated with motor adaptation match those predicted by adaptation related to the actual movement, rather than the planned movement. At first glance, these results seem to contradict the results of Hirashima and Nozaki [10]. However, one could speculate that, if the actual movement one learns includes the movement of the displayed cursor, the formation of distinct internal models could be possible.

Although it is often assumed that the interference seen in A – B – A motor learning paradigms arises because of a limitation in learning multiple internal models, Krakauer and colleagues [14] have suggested an alternative account: that interference arises from a limitation in retrieving the correct model from memory. This, of course, is a well-established phenomenon in other areas of learning and memory and has a history within psychology dating back over 100 years to the seminal work of Ebbinghaus [17] and Bergstrom [18]. Within this framework, the deficits observed when participants attempt to learn two distinct internal models for a single set of movement kinematics are not a result of a difficulty in creating the model, but rather result from interference that occurs at the time of model retrieval. In the typical A – B – A paradigm, the same goal in visual space becomes associated with two possible internal models, with few cues available to guide the appropriate recollection. In explaining the results of Hirashima and Nozaki [10], such a framework would suggest that the presence of two goals in extrinsic space provides a definitive memory cue allowing the recall of the appropriate internal model at the appropriate time. However, it is unclear why the location of the target in the work of Hirashima and Nozaki [10] would act as a sufficient memory cue, when features such as the shape, color, size and even the location on the body to which the perturbation is applied have all had limited success as contextual cues in the learning and/or retrieving of distinct internal models [6,19,20].

In summary, the new work of Hirashima and Nozaki [10] effectively demonstrates that the motor system is more flexible than previous studies have suggested when it comes to adapting to novel environments. Further, this is an exciting time for the field, with a number of testable hypotheses coming to light, providing a multitude of plausible frameworks to explain these new research findings. In addition to theoretical accounts, future research will no doubt begin to identify the neurological systems that are responsible for this new found ability and will invariably provide knowledge that could have a wide-ranging impact on understanding typical and atypical human motor performance, robotic control systems, and rehabilitation regimens.

References

1. Tseng, Y.W., Diedrichsen, J., Krakauer, J.W., Shadmehr, R., and Bastian, A.J. (2007). Sensory prediction errors drive cerebellum-dependent adaptation of reaching. J. Neurophysiol. *98*, 54–62.
2. Flanagan, J.R., Bowman, M.C., and Johansson, R.S. (2006). Control strategies in object manipulation tasks. Curr. Opin. Neurobiol. *16*, 650–659.
3. Shadmehr, R., and Mussa-Ivaldi, F.A. (1994). Adaptive representation of specific dynamics during learning of a motor task. J. Neurosci. *14*, 3208–3224.
4. Wolpert, D.M., Diedrichsen, J., and Flanagan, J.R. (2011). Principles of sensorimotor learning. Nat. Rev. Neurosci. *12*, 739–751.
5. Shadmehr, R., Smith, M.A., and Krakauer, J.W. (2010). Error correction, sensory predictiom, and adaptation in motor control. Annu. Rev. Neurosci. *33*, 89–108.
6. Gandolfo, F., Mussa-Ivaldi, F.A., and Bizzi, E. (1996). Motor learning by field approximation. Proc Natl. Acad. Sci. USA *93*, 3843–3846.
7. Caithness, G., Osu, R., Bays, P., Chase, H., Klassen, J., Kawato, M., Wolpert, D.M., and Flanagan, J.R. (2004). Failure to consolidate the consolidation theory of learning for sensorimotor adaptation tasks. J. Neurosci *6*, 8662–8671.
8. Osu, R., Hirai, S., Yoshioka, T., and Kawato, M. (2004). Random presentation enables subjects to adapt to two opposing forces on the hand. Nat. Neurosci. *7*, 111–112.
9. Nozaki, D., Kurtzer, I., and Scott, S.H. (2006). Limited transfer of learning between unimanual and bimanual skills within the same limb. Nat. Neurosci. *9*, 1364–1366.
10. Hirashima, M., and Nozaki, D. (2012). Distinct motor plans form and retrieve distinct motor memories for physically identical movements. Curr. Biol. *22*, 432–436.
11. Thoroughman, K.A., and Shadmehr, R. (2000). Learning of action through adaptive combination of motor primitives. Nature *407*, 742–747.
12. Donchin, O., Francis, J.T., and Shadmehr, R. (2003). Quantifying generalization from trial-by-trial behavior of adaptive systems that learn with basis functions: throy and experiments in human motor control. J. Neurosci. *23*, 9032–9045.
13. Hwang, E.J., Donchin, O., Smith, M.A., and Shadmehr, R. (2003). A gain-field encoding of limb position and velocity in the internal model of arm dynamics. PLoS Biol. *1*, 209–220.
14. Krakauer, J.W., Ghez, C., and Ghilardi, M. (2005). Adaptation to visuomotor transformations: Consolidation, interference, and forgetting. J. Neurosci. *12*, 473–478.
15. Smith, M.A., Ghazizadeh, A., and Shadmehr, R. (2006). Interacting adaptive processes with different timescales underlie short-term motor learning. PLoS Biol. *4*, e179. 10.1371/journal.pbio.0040179.
16. Gonzalez Castro, L.N., Monsen, C.B., and Smith, M.A (2011). The binding of learning to action in motor adaptation. PLoS Comput. Biol. *7*, e1002052. 10.1371/journal.pcbi.1002052.
17. Ebbinghaus, H. (1913). Memory: A Contribution to Experimental Psychology (New York: Teachers College, Columbia University).
18. Bergström, J.A. (1894). The relation of the interference to the practice effect of an association. Am. J. Psychol. *6*, 433–442.
19. Corthos, N., Wong, J., and Gribble, P. (2008). Distinct haptic cues do not reduce interference when learning to reach in multiple force fields. PLoS One *3*, e1990, 1910.1371/journal.pone.0001990.
20. Davidson, P.R., Wolpert, D.M., Scott, S.H., and Flanagan, J.R. (2005). Common encoding of novel dynamic loads applied to the hand and arm. J. Neurosci. *25*, 5425–5429.

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Sliding Clamps: An Open and Shut Case?

Molecular events in the clamp-loading reaction pathway of DNA replication are revealed by new crystal structures of bacteriophage T4 clamp