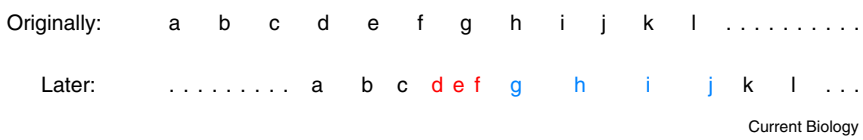

Figure 2. Effect of secular variation on the gradient of a magnetic parameter.

Top line: this idealized beach has, initially, an evenly spaced set of parameter values (intensity or inclination) running from left to right (west to east, say). Bottom line: with the passage of time the locations with these particular parameter values will have drifted in a non-linear way, leading to regions where the values are clumped (red) or dispersed (blue). Nesting density tracks this shift.

geographical location and the one currently designated by the pair of magnetic parameters — a particularly useful update if the apparent target has moved inland. The imprinting/remigration alternatives can only be resolved by tracking individuals, a task that necessarily involves waiting a couple of decades for hatchlings to mature and nest twice — a heroic (and unlikely) undertaking.

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Motor Neuroscience: Changing the Future and Remembering the Past

A new study shows that two skills that would otherwise interfere can be learned if each has a unique following action, and that a single skill is learned more quickly if the goal of the subsequent action is consistent across trials.

Chris Miall

What factors constrain the acquisition and retention of a motor behavior or skill? Many studies explore these issues by measuring the interference caused by learning two incompatible tasks, as a probe of the retention of one motor memory in the face of another competing one. In this issue, Howard *et al.* [1] report that participants can compensate for two different and conflicting perturbations in a reaching task, if a subsequent movement provides a cue to disambiguate the two conditions. This implies that the context in which we learn a skill includes not only current and past actions [2] but also future actions.

Motor skills are learned and refined based on movement outcomes. This process normally combines reinforcement learning, where success is signaled by reward and influences future action choices, and error-correction, where feedback directs performance changes to reduce subsequent errors. Both types of learning depend on a memory trace of a recent action, which can be used to attribute responsibility to the action for any reward or error. These two processes gradually alter the neural representation of the motor actions — often referred to as an internal model [3] — and the improved performance is taken as a measure of acquired 'skill'.

How then is it possible to learn two different but similar skills? Why don't these learning processes degrade existing skills while improving newly learned ones? For example, the leg movements involved in cycling or dancing are not very distinct from those used in walking, and share similar neural control circuits. But luckily we do not forget how to walk when we learn to cycle or dance; in fact locomotor control is so flexible that we can learn direction specific walking patterns in the lab that we would never encounter in our normal environment [4,5]. Other examples abound — tennis and squash, typing and piano playing, and so on.

However, there are also striking counterexamples, in which apparently simple tasks simply don't get learnt. In 2002, Karniel and Mussa-Ivaldi [6] reported that people quickly learn to move a robotic handle to a target despite their arm being perturbed by a lateral force, but if the direction of the force is alternated on every trial, left and right, they just don't learn. This remarkable failure to learn in the face of a simple task can be attributed to the dumb process of error correction: if on one trial the force is leftward, then on the next trial the participant should try to move more towards the right; if this coincides with a reversal of the force field, then moving rightwards makes things worse rather than better, and there is an even bigger overshoot. With less frequent switches, both conditions are learned, albeit slowly, as there are repeated errors under the same condition [7]. If the conditions are presented in blocks, with hundreds of trials with one perturbation before each reversal, participants learn each condition well, but have to repeatedly learn and relearn.

So learning one skill often does block retention of another — the error-corrections in one condition affect the memory of actions established in the previous condition [8]. A contextual cue is then required to allow the two conditions to be separated, so that one is learnt without erasing the other. With cues

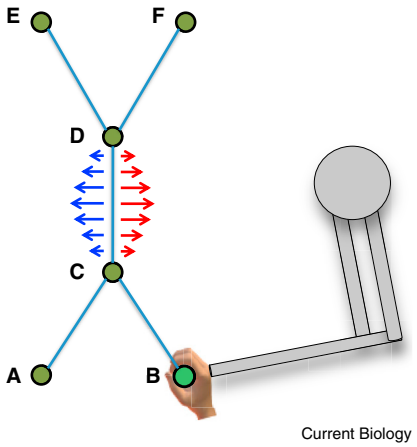

Figure 1. Separation of learning context by past and future actions.

The movement task used by Howard *et al*. [1] required participants to move a motorized handle between central start and target locations (C and D), in the face of forces generated by the handle pushing them off-course. If the force on each trial randomly pushed them left (blue) or right (red), the participants could not learn to compensate. If the lead-in action (AC or BC) uniquely cued the force, then participants were able to learn [2]. The authors now show [1] that the follow on actions (DE or DF) also act as cues, and that complex combinations such as the exclusive-OR between lead-in and follow on can be solved.

[8], or with sufficient time between exposure to the opposing tasks [9], the memories of each can be consolidated independently [8]. Interestingly, more recent studies show that if successful movements in one condition are rewarded (with a positive bleep, or the award of a point), then this reinforcement signal seems to help stabilize the new skill and forms a new baseline [10]. After such reinforcement, future error-driven learning is from — and future forgetting is back towards — this new baseline. There is now a great deal of effort across many laboratories dedicated to sorting out the complex interactions between actions and outcomes, error-correction and reinforcement, and skill acquisition and memory retention.

In a pair of recent studies [1,2], including the one reported in this issue, Howard and colleagues addressed a closely related question — what is the unit of movement that forms a singular action or memory that is associated with one outcome? They first reported [2] that participants could indeed learn to compensate for two alternating force fields — unlike the result reported by Karniel *et al.* [6] — if each action performed in the force field proceeded from an earlier and distinct lead-in movement. In other words, participants could learn to disambiguate left versus right forces if they moved from two different starting positions (path AC or BC in Figure 1) during the lead-in to the perturbed part of each trial (path CD). The authors demonstrated that one action could be tied to a following action and provide a contextual cue to the condition coming up, and found that an interval of about 600 ms or more was needed to uncouple the two sub-parts [2]. After 600 ms the first action didn't provide a memory trace useful to the second action.

In the new paper [1], the authors extend this work by showing that the follow-on after the perturbed section of a trial can also disambiguate different force conditions (paths DE or DF in Figure 1). In other words, a single 'action' trace that is associated with an outcome (an error caused by the perturbing force-field) can combine a lead-in movement, an ambiguous middle phase, and a follow-on movement. This combination allowed their participants to distinguish complex conditions including an exclusive-OR, where the direction of the force-field experienced in the middle phase (path CD) depended on both the lead-in action and the follow-on action, and could only be solved by using both as cues. It seems counterintuitive, but what we do next affects what we remember now. As time only flows forwards, what we remember now must affect how we represent what we will do next.

What are the implications? Howard *et al.* [1] suggest these results might explain the follow-through actions in ball sports, where it is known that practicing to hit a ball with a consistent swing-through enhances skill learning. This interpretation stretches beyond what they have tested, because in a sporting context, it is often the momentum of the arm, leg or racquet that contributes to the follow-through rather than the need to reach a particular location. Also, their experiment suggests that a consistent goal for the follow-through provides the important contextual cue, perhaps more than the consistent performance of the action towards that goal. But their results also imply that the contextual relationships between movements are short lived. The authors have not yet explored actions as contextual cues in reinforcement learning, but these connections are likely within this framework too. Any agent in natural learning conditions faces the challenge of understanding the relationships between a series of actions that ultimately lead to a reward, rather than just the final action in the chain [11]. It would be very difficult to learn complex tasks if each action needed to be performed within just 600 ms of each other to be linked as a sequence. The memory traces of contextual cues in reinforcement and in error correction may be quite different.

It is also interesting to think what these results tell us about working memory for actions. Sequences of simple actions like button presses or piano keyboard notes are chunked into smaller, more memorable sections. Are sequences of reaching movements also bound together as a contextual unit, or chunk? If so, what is the upper size limit, and does this load on working memory itself constrain learning [12,13]? Working memory capacity is about seven items [14] — for observed actions it seems much smaller [15], so one might expect a low upper limit.

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Cell Biology: Cohesin Rings Leave Loose Ends

Cohesins function in almost all aspects of chromosome biology. Two new studies confirm that a subset of cohesin subunits form a flexible but compressed ring that can be opened through degradation. X-ray crystallography supports potentially differing regulation of subunit associations.

Robert V. Skibbens

Prior to dividing, the cell copies its genetic material to produce two identical sets of chromosomes that are termed sister chromatids. The time interval between replicating the genome (S phase of the cell cycle) and segregating the sister chromatids into newly forming daughter cells (M phase of the cell cycle) can be hours, months or even years. Given that our genomes are chock full of repeated DNA sequences, gene families and oft-used motifs, identifying over time which chromatids are sisters can be a sticky business. The solution appears simple: glue sisters together from the time of synthesis until segregation. Elucidating both the structure of that glue, a protein complex termed cohesin, and mechanisms through which cohesins are regulated fostered a diversity of models [1]. Resolving these models is of significant interest given that cohesins are also critical for chromosome condensation, DNA replication and repair, ribosome maturation and proper deployment of transcription programs (Figure 1A) [2]. Notably, mutations in cohesin can result in aneuploidy (a characteristic of cancer cells), severe developmental maladies, or both [3]. Two articles published in *Science* by Gligoris and colleagues and Huis in 't Veld and colleagues solidify an expansive body of evidence that three cohesin subunits, Mcd1(Scc1/RAD21), Smc1 and Smc3, form a closed ring [4,5]. X-ray crystallographic analysis of a subset of cohesin interactions further suggest that, while SMC proteins are highly conserved, Mcd1 binds to distinct domains within Smc1 and Smc3, suggesting that each association may be differentially regulated during cohesin–DNA interactions. Here, I discuss the broader implications of the cohesin ring and why the study of cohesin remains in its infancy.

What Does Structure Have To Do with It?

At least five proteins are required to maintain sister chromatid cohesion: Smc1, Smc3, Mcd1(Scc1/RAD21), Scc3(Irr1/SA1,2) and Pds5 (all capitals denote vertebrate proteins). Vertebrate cells contain a sixth cohesin-binding factor, Sororin, which is also essential for cohesion. Early findings in yeast revealed that cohesins are recruited to DNA during S phase and subsequently converted to a cohesion-competent state by the S phase factor Ctf7/Eco1. Interactions between Ctf7/Eco1 and PCNA (DNA replication processivity factor) and other studies thus led to the model that cohesion is established through the tethering together of cohesins bound on each sister [6]. Structural analyses of cohesins, however, significantly altered the cohesion landscape [7–10]. SMC proteins are elongated proteins (~100 nm) that fold in half at a centrally located hinge. Anti-parallel coiled coils extend from the hinge, bringing globular amino and carboxyl termini in registration to form an ATPase head domain. Smc1,3 proteins dimerize through hinge–hinge interactions on one end with additional evidence that Smc1,3 heads transiently associate at the other end. Smc1,3 head associations are capped (or bridged) by Mcd1 to form a contiguous ring. In turn, Mcd1 recruits Scc3 and Pds5 (Figure 1B). Similar to other cohesin subunits, Scc3 and Pds5 are essential for cohesion even though they do not participate in the contiguous ring structure [11]. The notion that cohesins form a ring spawned an 'entrapment' model of cohesion. If cohesin rings could be deposited on DNA before S phase, then subsequent passage of the DNA replisome would entrap both sister chromatids [8,9]. In pursuing this model, Huis in 't Veld and colleagues examined transmission electron microscopy (TEM) micrographs of recombinant dimeric (SMC1,3) and tetrameric (SMC1,3, SA1 and Mcd1/RAD21) human cohesins, focusing on complexes in which elongated coiled-coil structures were easily discernible. SMC1,3 dimers (tethered together by hinge–hinge association) form flexible and often open (SMC1,3 heads apart) structures, although a significant population of dimers retained SMC1,3 head interactions. In contrast, tetrameric cohesins formed a closed ring-like structure with SMC1,3 heads capped by Mcd1 that were uniformly positioned ~25 nm apart [5]. In the adjoining article, Gligoris and colleagues analyzed cohesins assembled *in vivo*. Here, the authors modified each of the three subunit interfaces (Mcd1–Smc3, Smc3–Smc1 and Smc1–Mcd1) to allow for inducible covalent cross-links that resist detergent denaturation. Indeed, cross-links produced structures that migrated during gel electrophoresis as trimeric complexes, indicative of a closed ring [4]. Thus, both studies