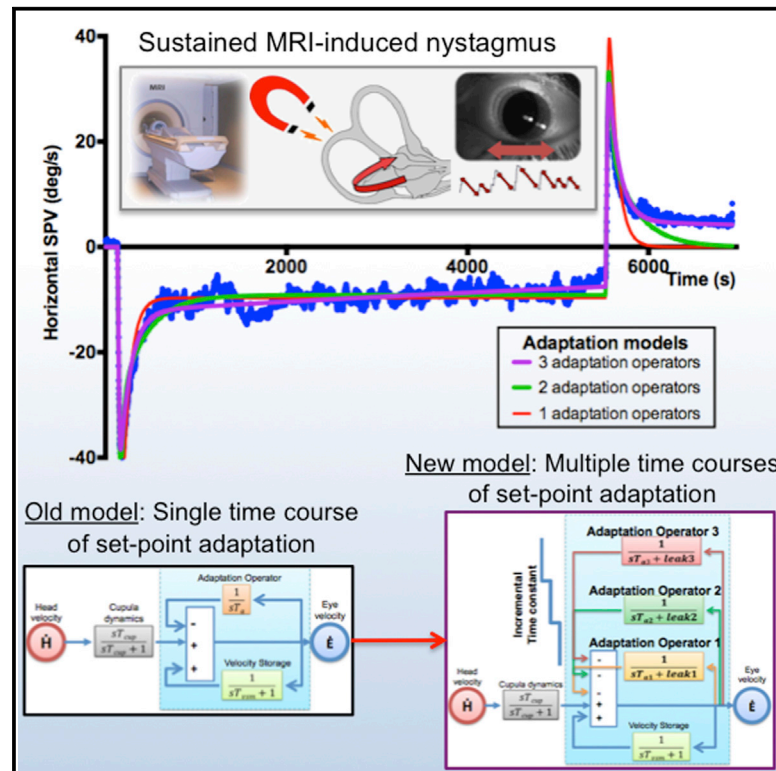


# Current Biology

## Multiple Time Courses of Vestibular Set-Point Adaptation Revealed by Sustained Magnetic Field Stimulation of the Labyrinth

### Graphical Abstract



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### In Brief

Jareonsettasin et al. use 90-min MRI labyrinthine stimulation to elicit vestibular nystagmus and study set-point adaptation—how neural activity is rebalanced to ensure stable platforms for movement. They found multiple timescales of learning and developed a model in which a cascade of imperfect integrators acts toward removing an unwanted bias.

### Highlights

- MRI vestibular stimulation acts as head acceleration, producing sustained nystagmus
- After 90-min exposure, the presumed pathological nystagmus is partially removed
- Multiple adaptation time courses are shown, reflecting set-point (bias) adaptation
- We propose a cascade of imperfect integrators of progressively slower dynamics



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## SUMMARY

A major focus in neurobiology is how the brain adapts its motor behavior to changes in its internal and external environments [1, 2]. Much is known about adaptively optimizing the amplitude and direction of eye and limb movements, for example, but little is known about another essential form of learning, “set-point” adaptation. Set-point adaptation balances tonic activity so that reciprocally acting, agonist and antagonist muscles have a stable platform from which to launch accurate movements. Here, we use the vestibulo-ocular reflex—a simple behavior that stabilizes the position of the eye while the head is moving—to investigate how tonic activity is adapted toward a new set point to prevent eye drift when the head is still [3, 4]. Set-point adaptation was elicited with magneto-hydrodynamic vestibular stimulation (MVS) by placing normal humans in a 7T MRI for 90 min. MVS is ideal for prolonged labyrinthine activation because it mimics constant head acceleration and induces a sustained nystagmus similar to natural vestibular lesions [5, 6]. The MVS-induced nystagmus diminished slowly but incompletely over multiple time-scales. We propose a new adaptation hypothesis, using a cascade of imperfect mathematical integrators, that reproduces the response to MVS (and more natural chair rotations), including the gradual decrease in nystagmus as the set point changes over progressively longer time courses. MVS set-point adaptation is a biological model with applications to basic neurophysiological research into all types of movements [7], functional brain imaging [8], and treatment of vestibular and higher-level attentional disorders by introducing new biases to counteract pathological ones [9].

## RESULTS

### Experimental Rationale and Protocols

To study set-point adaptation, we opted for a vestibular model since the unwanted spontaneous nystagmus that occurs after a unilateral labyrinthine lesion is an archetypical problem for the adaptation networks that adjust set points; they must restore balance centrally to overcome any persistent asymmetrical activity arriving from the periphery [10]. This nystagmus normally dissipates over time through adaptive processes [11, 12]. Using the effects of magnetic fields on the labyrinth of normal humans (magneto-hydrodynamic vestibular stimulation [MVS] due to Lorentz forces that act on fluids within the semicircular canals and push the cupula to a new position [5, 6, 13]), we created a surrogate vestibular lesion to study set-point adaptation. MVS is especially suited to study vestibulo-ocular reflex (VOR) set-point adaptation given current ideas that MVS simulates constant head acceleration and produces a sustained nystagmus. Because of properties of the labyrinth, and a central velocity-storage mechanism [14], the slow-phase velocity (SPV) induced by a constant acceleration should rise to a constant value with a time constant of 10–15 s [15, 16]. During sustained MVS, however, after reaching a maximum value, SPV slowly decays back toward a new but non-zero baseline. An adaptive process, inferring that sustained unchanging nystagmus is unnatural and pathological, supervenes toward eliminating the bias and unwanted eye drift. When the adaptive stimulus is abruptly removed, an aftereffect emerges with oppositely directed slow phases, revealing the prior adaptation.

### Adaptation Paradigms

Nine healthy normals (seven males, two females; 21 to 65 years) were studied in a 7T MRI. MRI protocols and video eye movement recordings and analysis were as in earlier papers [6, 17, 18]. After obtaining baseline data, the subject was moved into the MRI bore center and remained there for fixed durations between 5 s and 90 min. Afterward the subject was moved out of the bore to the starting position and remained still while the reversal nystagmus was recorded. Vestibular nystagmus was also elicited with en

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