inhibitory segment of the polypeptide that was blocking the active site. Detachment of this segment led to an exposure of the catalytic cleft allowing binding of ATP. Consistent with these data, independent biochemical experiments with a recombinant kinase expressed without the inhibitory segment confirmed that the kinase is capable of the autophosphorylation of its tyrosine residue, thus completing activation.

The new results thus provide experimental support of the earlier work and are fascinating in showing directly, and at the single molecule level, how changes in mechanical tension can regulate titin kinase activity. A similar mechanism may operate in regulation of giant titin-like kinases in invertebrate muscle [12]. Reversible changes in the length of myosin filaments [13–15], in the filament lattice spacing [16], or in shear tension [17] during muscle function are possible ways in which the titin kinase may be stretched in the sarcomere. However, detailed testing of the conclusions drawn from the results of Puchner *et al.* [4] requires a high resolution (~2 nm) model of the M-line structure where protein molecular shapes and their interactions can be recognized. Current structural M-line models [18] have ~5 nm resolution or worse, and biochemical schemes of M-line structure based on protein–protein interaction data are fragmentary [19,20]. Nevertheless, the speed of progress of new biochemical, single-molecule-mechanics and electron microscope techniques suggests such a thorough understanding may not be too far away.

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Speech Production: How Does a Word Feel?

Given the importance of auditory feedback in vocal production, how can deaf individuals produce intelligible speech? A new study suggests that somatosensory feedback is the answer and, more generally, offers intriguing insights into the action-oriented nature of sensory representations in the brain.

Asif A. Ghazanfar and Hjalmar K. Turesson

The 17th century philosopher John Locke (1632–1704) distinguished between ideas that humans acquire through a single sensory modality, vision for example, and those acquired through more than one modality [1]. He argued that individuals who lack a sense will never be able to acquire ideas that specifically relate to that sense: for example, the blind will never know the 'color' of anything. Other ideas, such as shape and motion, are acquired through multiple modalities and their combination, and can be aquired in the absence of any one sense. Intrigued by these ideas, a contemporary of Locke's, the scientist and politician William Molyneux (1656–1698), wrote to ask him whether a blind person who can distinguish between a cube and globe by touch could distinguish and name these objects by sight if his vision were to be suddenly restored. This question,

now known as 'Molyneux's Problem', continues to vex philosophers and scientists.

A parallel puzzle is evident in speech production. Human vocalizations involve exquisite control over the laryngeal, articulatory and respiratory musculature [2]. To produce speech, the motor system learns and maintains neural maps of the relationship between muscles, motor commands and sensory feedback. We know that auditory feedback is necessary for the acquisition of speech during development and, more recently, it has been established that it is necessary for the maintenance of speech in adults [3,4]. Here is the conundrum: intelligible speech is produced by individuals who become deaf as adults, even many years after they have not heard a thing. How is this possible? A new study by Nasir and Ostry [5] suggests that a natural form of sensory substitution [6] may be involved — that *somatosensory* feedback, generated by mechanoreceptors when different parts of the vocal tract move to produce speech, can assume the role of auditory feedback in deaf individuals.

Nasir and Ostry [5] tested speech motor learning in post-lingually deaf adults with their cochlear implants or hearing-aids turned off. A robotic device applied a mechanical load to the jaw as subjects repeated words — 'saw', 'say', 'sass' and 'sane' — appearing on a video monitor. This load was velocity dependent and displaced the jaw so that it caused a slight protrusion, thereby altering somatosensory feedback. Learning was assessed by measuring adaptation in the jaw trajectory. After hundreds of repetitions, the deaf individuals' trajectories adapted, becoming more similar to the trajectories seen before the load was applied. The subjects also showed an after-effect — in essence, an exaggerated jaw movement — when the load was unexpectedly removed. Such adaptation and after-effects were similar between deaf individuals and age-matched control subjects, but the sensory feedback could not be the same between these two groups. Individuals with normal hearing could guide their learning through auditory feedback, somatosensory feedback or both. Remarkably, learning by deaf individuals with their implants turned off could be mediated only by somatosensory feedback. Thus, auditory input is not *necessary* for speech learning in adults [5].

Two interesting questions (among many) come to mind in light of these findings. First, what is the nature of the neural representation underlying speech production? Given the influence of sensory feedback on motor adaptation, a simple feed-forward motor program is an unlikely candidate. Furthermore, both auditory and somatosensory modalities can have an influence. Thus, the neural representation of speech production is a multisensory-motor one and calls to mind what the philosopher Andy Clark [7] refers to as 'action-oriented' representations. In generic terms, action-oriented representations simultaneously describe aspects of the world and prescribe possible actions. They are poised between pure control (motor) structures and passive (sensory) representations of the external world. For neural representations of speech production, this suggests that the laryngeal, articulatory and respiratory movements during speech are inseparable from auditory and somatosensory feedback during the process of learning. Nasir and Ostry [5] show this to be true. A corollary of the action-oriented representation is that the learning process is very specific: learning one sensorimotor speech act does not necessarily generalize to other speech acts in different contexts. Two recent studies [4,8] of speech learning also suggest that this may be true.

This leads us to the second question: how might such a representation be instantiated in real neuronal networks? One likely node in such a network is the auditory cortex which receives a convergence of all the necessary signals for the speech learning described by Nasir and Ostry [5]. Recent work using a non-human primate model system revealed that auditory cortical neurons are not only strongly influenced by the production of vocal signals [9], but are sensitive to changes in auditory feedback during vocal production [10]. Somatosensory inputs also converge on auditory cortex in primates [11]. Furthermore, for the vast majority of auditory cortical neurons with somatosensory responses, the tactile receptive fields are confined to the head and neck area (areas associated with the vocal tract and larynx). Intriguingly, these data from nonhuman primates suggest that the auditory cortex may be a locus for aligning somatosensory feedback with auditory feedback during vocal production.

Human speech is often viewed as exclusively revolving around sounds, how we produce them and how we perceive them. Production of speech is seen as a pure motor act, involving muscles and the neurons controlling them, while perception of speech is seen as purely sensory, involving the ear and the auditory pathway. This parcellation of the systems appears intuitive and clear, but recent studies, including Nasir and Ostry's [5], suggest that such divisions may be fundamentally wrong [12,13]. Rather than separate processes for motor outputs and individual sensory modalities, adaptive action seems to use all the available context-specific information. That is, neural representations across the brain may be centered on specific actions. This view on neural representations puts 'Molyneux's Problem' in a new light. Unisensory signals are fused into multisensory motor representations unified by an action, but since Molyneux does not suggest any action, his 'problem' may be better viewed as an ill-posed question — at least from a neuroscientific perspective.

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Skotomorphogenesis: The Dark Side of Light Signalling

The ability to switch from skotomorphogenic to photomorphogenic development is essential for seedling survival. Central to this mechanism are the phytochrome interacting factors that are important for maintaining the skotomorphogenic state and regulating the switch to photomorphogenesis.

Eve-Marie Josse and Karen J. Halliday

Seedlings kept in darkness adopt a skotomorphogenic program of development, in which allocation of resources is typically directed toward hypocotyl elongation at the expense of cotyledon and root development. Rapid and exaggerated elongation of the hypocotyl provides a means for the seedling to seek light. The tightly folded apical hook allows easy passage through soil or other substrates and protects the small unfolded cotyledons and underlying meristematic region from damage. This growth strategy ensures that limited seed reserves are used economically and are devoted to the quest for light, a prerequisite for photoautotroph survival.

In a recent issue of *Current Biology*, Leivar *et al.* [1] illustrate how the balance between skotomorphogenesis and photomorphogenesis is achieved during *Arabidopsis* seedling establishment. Central to this process are the phytochrome interacting factor (PIF) transcription factors, key modulators of the dark, etiolated state.

In darkness, skotomorphogenesis is achieved by the active repression of the genes that would lead to de-etiolation and photomorphogenic development. This process is regulated by the COP1–SPA1 E3 ligase complex that targets transcription factors like HY5 for degradation by the proteasome [2]. Leivar *et al.* [1] have demonstrated that an accompanying PIF-dependent mechanism is necessary to regulate gene transcription, hypocotyl cell elongation and maintenance of the etiolated state.

It is now well established that the PIF subgroup of basic helix-loop-helix transcription factors comprises important light signalling components. A key feature of the *pif* knock-out phenotype is exaggerated de-etiolation, indicating that these transcription factors antagonise de-etiolation in light-grown seedlings [3]. The closely related PIF1, PIF3, PIF4 and PIF5 have been shown to preferentially interact with the active, Pfr form of the phytochrome B (phyB) light receptor through the conserved active phytochrome binding (APB) motif [4]. Following light activation of phyB, a strong promoter of de-etiolaton, PIFs are phosphorylated and targeted for proteolytic degradation by the proteasome [5–8]. These studies suggest that the phyB–PIF module can provide a potent 'lights on' signal that leads to rapid changes in gene transcription as a result of phyB-induced depletion of PIF levels. However, recently, the validity of this model has moved under the spotlight with the finding that, under constant light conditions, *pif* mutant phenotypes may result directly from PIF feedback modulation of phyB levels [9–11]. Leivar *et al.* [1] have now provided strong support for the former model operating in emerging, dark-grown seedlings. This phyB–PIF mechanism provides a means to maintain the etiolated state, yet it is primed to respond to light.

The notion that PIFs actively regulate genes that maintain etiolated development predicts that mutants deficient in PIFs will display a constitutive-photomorphogenic (cop)-type phenotype in the dark. Leivar *et al.* [1] have demonstrated that this is indeed the case. Mutants deficient in individual PIFs have relatively mild, or poorly penetrative cop phenotypes. However, in seedlings with deficiencies in two or more PIFs, the phenotype is more striking. Indeed, PIF1, PIF3, PIF4 and PIF5 all appear to contribute to the maintenance of the dark-grown etiolated state.

To probe the roles of PIFs in maintaining etiolated development, Leivar and co-workers [1] employed a commonly utilised set-up protocol for dark-grown seedlings. In this standard protocol, seeds are exposed to two brief periods of light, the first during plating and the second post-stratification (4°C cold treatment), in an otherwise dark environment. By manipulating the amount of phytochrome activated by each light pulse, the authors were able to dissect out the roles of phyB and PIFs in the emerging seedling.

The interdependence of temperature and light in breaking seed dormancy in fresh seed is exemplified in *Arabidopsis*. A cold stratification period followed by a light pulse provides a potent germination signal. Core to this signal are the light-stimulated degradation of PIF1 and the cold activation of SPT [12–14]. In addition to germination, Leivar *et al.* [1] have shown that light provided either during seed plating or post-stratification also imposes influence on the emerging seedling architecture. This influence of light is manifest in mutants with deficiencies in PIFs: they exhibit marked photomorphogenic traits, a phenomenon that was previously reported for the *pif1 pif3 pif4 pif5* quadruple mutant [15]. The residual light effects observed in dark grown seedlings were designated 'pseudo-dark' responses (Figure 1). PIF1 appears to play a prominent pseudo-dark role, particularly in response to the early light pulse, provided during seed plating.