to induce the generation of precise compensatory forces that counteract the unexpected loads [6]. What determines the relative contributions of these two types of response to disturbances is not completely understood, but work on limb control suggests that the balance of responses might vary over the course of learning. An initial response is to stiffen in the face of unfamiliar forces but then, if the disturbances are predictable, the CNS quickly also learns to produce opposing forces to counteract the disturbing force [16]. This learning can happen very rapidly with crude predictive responses seen even on the second trial [17].

The picture that is emerging of speech is one of an activity that is produced with the aid of rich, predictive motor representations that learn aspects of the task, performance environment and the feedback that is expected when an action is performed. For speech, this means that the sound system of the language, the individual vocal tract morphology, and the expected auditory and somatosensory feedback are contained in a motor representation that is drawn upon when a sound sequence is planned. In its reliance on these learned representations, speech motor control shows marked similarities to limb control [18]. In spite of the linguistic message being conveyed and the higher order influences on the form of this message, speech is in the end a motor activity; as Nasir and Ostry [7] report, this requires that the mechanical environment and dynamic stability of the final filter in the language production process, the speech musculature, be taken into account.

References

1. Perkell, J.S. (1969). Physiology of Speech Production (Cambridge, MA: M.I.T. Press).
2. Houde, J.F., and Jordan, M.I. (1998). Sensorimotor adaptation in speech production. Science *279*, 1213–1216.
3. Jones, J.A., and Munhall, K.G. (2005). Remapping auditory-motor representations in voice production. Curr. Biol. *15*, 1768–1772.
4. Purcell, D.W., and Munhall, K.G. (2006). Adaptive control of vowel formant frequency: Evidence from real-time formant manipulation. J. Acoust. Soc. Am. *120*, 966–977.
5. Tremblay, S., Shiller, D.M., and Ostry, D.J. (2003). Somatosensory basis of speech production. Nature *423*, 866–869.
6. Ito, T., Gomi, H., and Honda, M. (2004). Dynamical simulation of speech cooperative articulation by muscle linkages. Biol. Cybernet. *91*, 275–282.
7. Nasir, S., and Ostry, D.J. (2006). Somatosensory precision in speech production. Curr. Biol. *16*, 1918–1923.
8. Moll, K. (1960). Cinefluorgraphic techniques in speech research. J. Speech Hear. Res. *3*, 227–241.
9. Goldstein, L., and Fowler, C.A. (2003). Articulatory phonology: a phonology for public language use. In Phonetics and Phonology in Language Comprehension and Production, N. Schiller and A. Meyer, eds. (Berlin: Mouton de Gruyter), pp. 159–208.
10. Perkell, J.S., Guenther, F.H., Lane, H., Matthies, M.L., Perrier, P., Vick, J., Wilhelms-Tricarico, R., and Zandipour, M. (2000). A theory of speech motor control and supporting data from speakers with normal hearing and with profound hearing loss. J. Phonet. *28*, 233–272.
11. Guenther, F.H., Hampson, M., and Johnson, D. (1998). A theoretical investigation of reference frames for the planning of speech movements. Psychol. Rev. *105*, 611–633.
12. Perkell, J.S., Matthies, M.L., Tiede, M., Lane, H., Zandipour, M., Marrone, N., Stockmann, E., and Guenther, F.H. (2004). The distinctness of speakers' /s/-/S/ contrast is related to their auditory discrimination and use of an articulatory saturation effect. J. Speech Lang. Hear. Res. *47*, 259–269.
13. Shiller, D.M., Laboissiere, R., and Ostry, D.G. (2002). Relationship between jaw stiffness and kinematic variability in speech. J. Neurophysiol. *88*, 2329–2340.
14. Shiller, D.M., Houle, G., and Ostry, D.G. (2005). Voluntary control of human jaw stiffness. J. Neurophysiol. *94*, 2207–2217.
15. Ostry, D.J., Vatikiotis-Bateson, E., and Gribble, P.L. (1997). An examination of the degrees of freedom of human jaw motion in speech and mastication. J. Speech Lang. Hear. Res. *40*, 1341–1351.
16. Shadmehr, R., and Mussa-Ivaldi, F.A. (1994). Adaptive representation of dynamics during learning of a motor task. J. Neurosci. *14*, 3208–3224.
17. Milner, T., and Franklin, D. (2005). Impedance control and internal model use during the initial stage of adaptation to novel dynamics in humans. J. Physiol. *567*, 651–664.
18. Tin, C., and Poon, C.S. (2005). Internal models in sensorimotor integration: Perspectives from adaptive control theory. J. Neural Eng. *2*, S147–S163.

Department of Psychology, Department of Otolaryngology, Queen's University, Kingston, Ontario, Canada, K7L 3N6.
E-mail: Kevin.Munhall@queensu.ca

DOI: 10.1016/j.cub.2006.09.049

Meiotic Spindle: Sculpted by Severing

Katanin is a conserved AAA ATPase with the ability to sever microtubules, but its biological function in animal cells has been obscure. A recent study using electron tomography has found that katanin stimulates the production of microtubules in the meiotic spindles of *Caenorhabditis elegans* oocytes.

Katharina Ribbeck and Timothy J. Mitchison

The protein katanin earned its name by its ability to sever microtubules — katanin is the Japanese word for sword. It was discovered by biochemical purification from sea urchin embryos [1] and is widely conserved in animals and plants, but its biological functions have been difficult to elucidate. It is not obvious why cells need a microtubule-severing enzyme; microtubules mediate transport by providing long tracks for motor proteins to travel along, and they can grow and shrink rapidly from their ends, which should allow remodeling of the cytoskeleton without the need for severing. Experiments in neurons and plant cells have suggested that katanin trims microtubules into fragments that can be efficiently transported and orientated within the cytoplasm, facilitating morphogenesis of complex cytoskeletons [2–4]. These experiments used interphase cells, and did not explain an early observation that katanin activity is highly increased in *Xenopus* egg extract in M-phase relative to interphase, which pointed toward a mitotic function of katanin, such as rapid disassembly of interphase

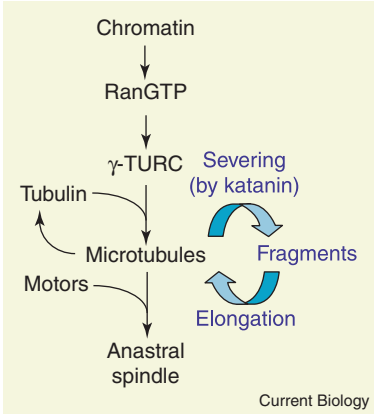

Figure 1. Possible pathway of anastral spindle assembly.

The current literature consensus is indicated in black. Chromatin recruits RCC1, triggering GTP exchange on Ran. In a poorly characterized step, this leads to activation of microtubule-nucleating complexes. Microtubules are nucleated, and subsequently organized into a bipolar spindle by motor proteins. Microtubules are unstable, and rapidly lost by dynamic instability. Blue indicates the proposed contribution of katanin. Severing followed by elongation of fragments amplifies microtubule number. The combination of amplification by severing with loss by depolymerization increases turnover of microtubules, and might facilitate spindle assembly by allowing kinetic proofreading of spatial location.

microtubules [5,6]. Studies using the nematode *Caenorhabditis elegans* showed that katanin is necessary during meiotic M-phase in oocytes, but not during mitotic M-phase in embryos. Indeed, inducing ectopic katanin expression in mitosis was found to damage the mitotic spindle [7]. This suggested that katanin might have a function specifically in oocyte meiotic spindles that is not shared with blastomere mitotic spindles. As reported recently in *Current Biology*, Srayko *et al.* [8] have now obtained strong evidence for a novel function of katanin — it appears to stimulate microtubule polymer production at the meiotic spindle.

Although oocyte meiotic spindles and blastomere mitotic spindles have similar chromosome segregation functions, they differ considerably in their organization. Blastomere spindles are dominated by a pair of spherical centrosomes, one at each pole, which rapidly nucleate an astral array of microtubules. Some of these interact with chromosomes to form the spindle, while others radiate outwards towards the cortex to position the spindle. Nucleation at centrosomes is catalyzed by γ-tubulin ring complexes (γ-TURCs), which structurally mimic the plus ends of microtubules [9]. Oocyte meiotic spindles, in *C. elegans* and many other animals, are anastral — they lack centrosomes or conspicuous asters at the poles. Anastral spindles are thought to assemble by an 'inside-out' mechanism: microtubules are nucleated near chromatin in response to RanGTP [10] and subsequently organized into a spindle-shaped array by motor proteins [11]. But how anastral spindles produce and maintain a high concentration of microtubules in the absence of centrosome-catalyzed nucleation is a key open question.

To investigate the function of katanin during meiosis, Srayko *et al.* [8] compared the organization of microtubules in meiotic spindles of wild-type and katanin-deficient *C. elegans* oocytes by electron tomography. This elegant method provides a detailed map of microtubule organization. It is based on high-pressure freezing to preserve detailed structure, followed by computational reconstruction of three-dimensional maps from multiple images of the same section at different tilt angles. The authors observed that, in the absence of katanin activity, both the number of individual microtubules in the spindle, and the amount of microtubule polymer, is significantly reduced. They conclude that katanin functions to increase steady-state microtubule number and total microtubule polymer in the anastral meiotic spindle.

Intuitively, severing by katanin should lead to the destruction of microtubule polymer rather than an increased amount. Srayko *et al.* [8] suggest a simple model to explain this paradox. If the microtubule fragments generated by katanin do not immediately depolymerize, they could instead act as seeds, adding tubulin at their plus ends, and thereby generating more microtubules and extra polymer in the spindle. In other words, katanin could amplify microtubule production by creating new templates for polymer growth. To date, theories of anastral spindle assembly have focused on the question of how microtubules are nucleated in the absence of centrosomes. The findings of Srayko *et al.* [8] suggest an alternative concept, where the major driver of microtubule production is not nucleation, but rather a combination of severing and elongation (Figure 1).

A mechanism for generating new filaments other than conventional nucleation is new to microtubule biology, but comparable mechanisms have been discussed for some time in actin biology. Severing of existing actin filaments by cofilin, followed by elongation of the resulting fragments on their fast-growing end, is thought to be an important mechanism for generating new filaments at the leading edge of motile cells (reviewed in [12]). Interestingly, cofilin catalyzes only disassembly in *Listeria* comet tails [13], implying the stability of severed fragments, and whether they elongate or shrink, may be differentially regulated.

Srayko *et al.* [8] also asked how ectopic expression of katanin damages blastomere mitotic spindles. They found that katanin activity reduces the average microtubule length when expressed in astral mitotic spindles, as it does in anastral meitotic spindles. But in the blastomere spindles the extra microtubules were shorter on average, and total microtubule polymer mass did not increase. This suggests that katanin-generated microtubule fragments may be unable to elongate in mitotic spindles, and points towards a difference in the stability of new plus ends in meiotic versus mitotic spindles. Why might these short microtubules damage the spindle? Perhaps they simply interfere with chromosome attachment, as kinetochore microtubules normally stretch all the way from the centrosome to the kinetochore in *C. elegans* bastomere mitotic spindles [14]. Alternatively, the astral spindle may

lack the motor activities required to organize the short microtubules into a bipolar array. In anastral spindles, kinesin-5, a tetrameric, bipolar motor, is thought to slide anti-parallel microtubules apart, promoting bipolar organization [15]. The *C. elegans* blastomere spindle is unusual in that it does not require kinesin-5 activity for its assembly [16], and perhaps this correlates with an inability to tolerate short microtubules.

Breaking a microtubule in the middle is a difficult task, and we do not know how katanin achieves it. Katanin consists of a catalytic 60 kDa ATPase domain and a non-catalytic 80 kDa domain, which together form hexameric rings, 14–16 nanometers in diameter [17], and it acts cooperatively during microtubule severing [1], suggesting that a large protein assembly is needed to initiate severing. Srayko *et al.* [8] correlate katanin activity with the presence of elongated gaps in microtubule walls, and propose that these represent an intermediate step in katanin-induced severing [8]. Cryo-electron microscopy of reconstituted severing reactions might help bridge the gap between the biochemistry and *in vivo* electron microscopy observations, and thus elucidate the mechanism.

The new work of Srayko *et al.* [8] opens many interesting questions. For example, how is katanin activity regulated in meiotic cells? Is it regulated by Cdc2-cyclinB kinase, by RanGTP, or both? Why do katanin-generated seeds elongate, rather than depolymerize rapidly from newly exposed plus ends, as is the case for plus ends generated in spindles by artificial severing with a microbeam or microneedle [18,19]? This might imply transient stabilization of plus ends by katanin, even as it breaks the microtubule wall. And on an applied note, does katanin play a role in spindle assembly in human cancer cells? We know that cancer cells assemble spindles using a poorly understood combination of the centrosome-driven astral pathway, and the chromosome driven anastral pathway [20]. Analyzing the function of katanin in cancer cells might help us understand their spindle assembly pathways better, and provide ideas for new drug targets.

References

1. McNally, F.J., and Vale, R.D. (1993). Identification of katanin, an ATPase that severs and disassembles stable microtubules. Cell *75*, 419–429.
2. Burk, D.H., Liu, B., Zhong, R., Morrison, W.H., and Ye, Z.H. (2001). A katanin-like protein regulates normal cell wall biosynthesis and cell elongation. Plant Cell *13*, 807–827.
3. Bichet, A., Desnos, T., Turner, S., Grandjean, O., and Hofte, H. (2001). BOTERO1 is required for normal orientation of cortical microtubules and anisotropic cell expansion in *Arabidopsis*. Plant J. *25*, 137–148.
4. Ahmad, F.J., Yu, W., McNally, F.J., and Baas, P.W. (1999). An essential role for katanin in severing microtubules in the neuron. J. Cell Biol. *145*, 305–315.
5. McNally, F.J., and Thomas, S. (1998). Katanin is responsible for the M-phase microtubule-severing activity in *Xenopus* eggs. Mol. Biol. Cell *9*, 1847–1861.
6. Vale, R.D. (1991). Severing of stable microtubules by a mitotically activated protein in *Xenopus* egg extracts. Cell *64*, 827–839.
7. Pintard, L., Kurz, T., Glaser, S., Willis, J.H., Peter, M., and Bowerman, B. (2003). Neddylation and deneddylation of CUL-3 is required to target MEI-1/Katanin for degradation at the meiosis-to-mitosis transition in *C. elegans*. Curr. Biol. *13*, 911–921.
8. Srayko, M., O'Toole, E.T., Hyman, A.A., and Mueller-Reichert, T. (2006). Katanin disrupts the microtubule lattice and increases polymer number in *C. elegans* meiosis. Curr. Biol. *16*, 1944–1949.
9. Aldaz, H., Rice, L.M., Stearns, T., and Agard, D.A. (2005). Insights into microtubule nucleation from the crystal structure of human gamma-tubulin. Nature *435*, 523–527.
10. Zheng, Y. (2004). G protein control of microtubule assembly. Annu. Rev. Cell Dev. Biol. *20*, 867–894.
11. Walczak, C.E., Vernos, I., Mitchison, T.J., Karsenti, E., and Heald, R. (1998). A model for the proposed roles of different microtubule-based motor proteins in establishing spindle bipolarity. Curr. Biol. *8*, 903–913.
12. DesMarais, V., Ghosh, M., Eddy, R., and Condeelis, J. (2005). Cofilin takes the lead. J. Cell Sci. *118*, 19–26.
13. Rosenblatt, J., Agnew, B.J., Abe, H., Bamburg, J.R., and Mitchison, T.J. (1997). Xenopus actin depolymerizing factor/cofilin (XAC) is responsible for the turnover of actin filaments in *Listeria monocytogenes* tails. J. Cell Biol. *136*, 1323–1332.
14. O'Toole, E.T., McDonald, K.L., Mantler, J., McIntosh, J.R., Hyman, A.A., and Muller-Reichert, T. (2003). Morphologically distinct microtubule ends in the mitotic centrosome of Caenorhabditis elegans. J. Cell Biol. *163*, 451–456.
15. Kapitein, L.C., Peterman, E.J., Kwok, B.H., Kim, J.H., Kapoor, T.M., and Schmidt, C.F. (2005). The bipolar mitotic kinesin Eg5 moves on both microtubules that it crosslinks. Nature *435*, 114–118.
16. Sonnichsen, B., Koski, L.B., Walsh, A., Marschall, P., Neumann, B., Brehm, M., Alleaume, A.M., Artelt, J., Bettencourt, P., Cassin, E., *et al*. (2005). Full-genome RNAi profiling of early embryogenesis in *Caenorhabditis elegans*. Nature *434*, 462–469.
17. Hartman, J.J., and Vale, R.D. (1999). Microtubule disassembly by ATP-dependent oligomerization of the AAA enzyme katanin. Science *286*, 782–785.
18. Spurck, T.P., Stonington, O.G., Snyder, J.A., Pickett-Heaps, J.D., Bajer, A., and Mole-Bajer, J. (1990). UV microbeam irradiations of the mitotic spindle. II. Spindle fiber dynamics and force production. J. Cell Biol. *111*, 1505–1518.
19. Tirnauer, J.S., Salmon, E.D., and Mitchison, T.J. (2004). Microtubule plus-end dynamics in Xenopus egg extract spindles. Mol. Biol. Cell *15*, 1776–1784.
20. Wadsworth, P., and Khodjakov, A. (2004). E pluribus unum: towards a universal mechanism for spindle assembly. Trends Cell Biol. *14*, 413–419.

Systems Biology, Harvard Medical School, 200 Longwood Avenue, WA 536, Boston, Massachusetts 02115, USA.
E-mail: Katharina_Ribbeck@hms.harvard.edu

DOI: 10.1016/j.cub.2006.09.048

Spider Silk: Thousands of Nano-Filaments and Dollops of Sticky Glue

Some spiders use glues while others deploy strands of fine filaments for fixing flies. Recent work has provided new insights into the mechanical properties of these nano-scale ropes.

Fritz Vollrath

A spider's web, typically in combination with a powerful poison [1], is its principal tool in the struggle for survival. It is a highly tuned, light-weight net-structure that relies heavily on skilful engineering and the fitting deployment of a most versatile material: the spider's famous silk. A typical web spider makes up to