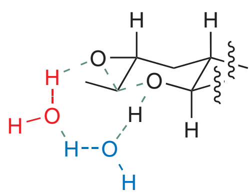
Dawn of auxin signaling

Because plants are stationary they require mechanisms such as the circadian clock to adjust to rapidly changing environmental conditions. Some 70 years ago, plant biologists observed a process termed 'gating' in which the growth response of plants to auxin, an endogenous plant hormone, was highly dependent on the time of day. A recent paper by Covington and Harmer now provides a mechanistic explanation for this effect. From gene expression profiles, the authors observed that approximately one tenth of the genes in *Arabidopsis thaliana* show periodic expression. Unlike genes associated with other plant hormones, genes involved in all aspects of auxin metabolism, from biosynthesis to transport and sensing, were tightly coupled to the circadian oscillator. Using an auxin-responsive luciferase gene expression assay, the authors showed that plants were most sensitive to auxin regulation during the 'late night' phase of the circadian cycle. This effect was not dependent on cyclic auxin biosynthesis or transport, but instead was related to downstream auxin sensing and signaling events. The direct effects of auxin on plant growth were similarly demonstrated to be under the control of the circadian clock. These results show the dominance of the circadian clock in regulating small-molecule signals and explain a decades-old phenomenon in plant biology; however, they also raise new questions about how plants use this cyclic pathway to mediate their interactions with their environment. (*PLoS Biology* **5**, 1773–1784, 2007) *TLS*

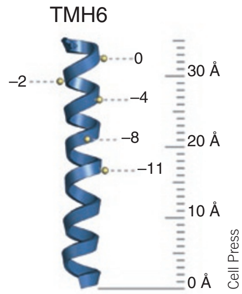
Rings on the rungs



Natural products have an inordinate number of different architectures, the formation of many of which have been explained or can be rationalized according to known biosynthetic logic. However, the creation of other natural products, such as polyether compounds with a 'ladder' topography, has eluded a full explanation as energetic considerations and model systems suggest that the observed products should not be formed. The Nakanishi cascade hypothesis posits that these ladder compounds could form via a cascade of epoxide rings opening. Vilotijevic and Jamison now provide the first experimental evidence in support of this long-standing hypothesis. Starting from a molecule that could perform a single step in the cascade, they observed that, in water, the pH of the system biases the size of the resultant ring, with an optimal pH of approximately 7 for formation of the desired six-membered ring. These conditions could be extended to molecules that undergo two or three individual cyclizations, with high yields and selectivity in each case. Other hydrogen bonding solvents such as methanol or ethylene glycol could similarly promote product formation emphasizing the importance of noncovalent interactions in the reaction. The unique geometries of the natural product mimics and the successful solvents suggest a potential mechanism in which a cooperative network of hydrogen bonds correctly positions the incoming nucleophilic oxygen for attack; this proposal now provides a concrete basis to investigate the enzymatic transformations of these intricate compounds. (*Science* **317**, 1189–1192, 2007) *CG*

Written by Catherine Goodman, Joanne Kotz & Terry L. Sheppard

Keeping chain length under control



Although most long fatty acids have chain lengths of 16 to 18 carbons, a portion of fatty acids are further elongated to 20 to 36 carbons. These very long-chain fatty acids (VLCFAs) are produced by an enzyme complex found in the membrane of the endoplasmic reticulum in a four-step enzymatic cycle that involves condensation of an acyl coenzyme A (CoA) precursor with malonyl-CoA, followed by reduction, dehydration and a second reduction to generate an acyl-CoA product with a chain that is extended by two carbons compared with the original substrate. The initial condensation and control of chain length is known to involve a family of elongase proteins (Elops), but the mechanistic details of the process were unknown until now. By reconstituting Elop activity in proteoliposomes, Denic and Weissman have demonstrated that Elops directly catalyze condensation through a noncanonical HXXHH motif. The authors fully reconstituted VLCFA biosynthesis by adding two known reductases, along with a dehydratase enzyme newly identified in this study, to active Elop. By varying the Elop in this *in vitro* system, the authors found that the condensing enzyme controls length not through substrate specificity, but by terminating iterative elongation cycles at a determined chain length. Through domain swapping and engineering experiments, the authors found that the position of a lysine on one face of a helical transmembrane domain directly controls the final chain length, which led the authors to propose a mechanism in which the length of the transmembrane domain functions as a 'caliper' to control VLCFA chain length. (*Cell* **130**, 663–677, 2007) *JK*

Monkey see, monkey count

The brain measures quantities such as brightness, number and size by integrating external information. However, the mechanism by which individual neurons participate in this process is unknown. To explore this idea, Tudusciuc and Nieder used matching tasks to train two rhesus monkeys to discriminate between different line lengths or numbers of dots (numerosity); behavioral responses demonstrated that the monkeys encoded these two quantities independently even though both tasks rely on measurement. To develop an increased understanding of the cellular basis of this result, the authors then analyzed the response of single neurons in matching tasks. Surprisingly, the authors observed that approximately 20% of neurons were preferentially discharged in response to a particular stimulus or during a subsequent delay (where the information had to be retained prior to display of the 'matched' response). Of these neurons, some only reported on length, whereas others only reported on numerosity. A final population was responsive to both sets of stimuli, but interestingly, the preferred 'size' (that is, 'long' or 'many') of the stimulus in one category did not correlate with a similar preference in the other category. By using a population decoding technique, the authors were then able to determine how the preferences of individual neurons could be integrated in small groups of neurons to provide the basis for one united 'thought'; this 'thought' is conveyed by parietal neurons based on a complex information code combining the classical firing rate with a temporal component. The ability of a small number of neurons to enact a sophisticated coding scheme provides new insights into the ways in which quantitative information is measured at the organismal level. (*Proc. Natl. Acad. Sci.* **104**, 14513–14518, 2007) *CG*