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► **COVER:** 'Decoding the mind' by Kirsten Lee, inspired by the review on p523.



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In many biological systems, there is a fine balance between stability and flexibility, and the brain's cells and circuitry are no exception. A major challenge faced by neurons and networks is to maintain long-term stability while there is a constant and rapid turnover in their underlying molecular components. Marder and Goaillard (page 563) provide a thought-provoking overview of the complex problems of compensating for variability in channel densities, synaptic strength and large networks, and reveal great flexibility in the solutions used to achieve robust neuronal and network behaviour.

The precise subcellular localization of ion channels is also fundamental to the successful functioning of neuronal networks. Lai and Jan (page 548) present a timely review of the literature on the localization in axons and dendrites of voltage-dependent ion channels and the molecular mechanisms by which they are maintained at these sites, illustrating important roles for trafficking, retention and endocytotic pathways.

Disruptions to normal ion channel function are associated with many neurological disorders, and the details of ion channel involvement in disease processes are the subject of intense study. For example, a Research Highlight on page 507 describes work that, for the first time, pinpoints gap junction hemichannels as the key players in neuronal death following ischaemic injury. Another highlight on page 508 reports the surprising finding that a single mutation to a voltage-gated sodium channel, associated with a neuropathic pain syndrome, produces entirely opposite phenotypes — hypo- or hyperexcitability — depending on the cell type in which it is expressed. Unravelling these important molecular and cellular mechanisms of neuronal and network function could take us a step closer to identifying therapeutic targets for a range of neurological disorders.

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on acid-free paper