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► **COVER:** 'Network' originally designed by Colleen Buzzard ([www.colleenbuzzard.com](http://www.colleenbuzzard.com)) and adapted by Erin Dewalt, inspired by the Focus on Signal Integration starting on p393.



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Cells process external cues through signalling pathways to respond to their environment, and pathway dysfunction is often associated with diseases. Cells must simultaneously integrate many signals to regulate responses to environmental changes, so understanding the crosstalk and interplay that occurs is essential when considering therapies that target signalling events.

We have teamed up with *Nature Structural & Molecular Biology* to present an in-depth joint Focus on Signal Integration ([www.nature.com/focus/signalintegration](http://www.nature.com/focus/signalintegration)), which examines the mechanisms of coordinating responses to signalling and the technical approaches to illuminating such complexity. Organismal development is an example of a process that requires integrated signalling events. To illustrate this, McNeill and Woodgett describe the Wnt and Hippo pathways, which are known to achieve considerable levels of diversity and selectivity through extensive integration and crosstalk (page 404). The study of certain signalling systems has started to reveal the underlying design principles, such as the spatiotemporal organization of signalling components, as Kholodenko, Hancock and Kolch discuss on page 414. Lim explains how these principles and others can be exploited to engineer cells with novel signalling behaviours for use in medicine and biotechnology (page 393).

Imaging technologies, combined with computational and theoretical models, have proved fundamental to elucidating how cells process signalling information, as Dehmelt and Bastiaens discuss on page 440. Similarly, large-scale 'precision proteomics' studies based on mass spectrometry have enabled a system-wide and quantitative characterization of signalling events (Choudhary and Mann, page 427). Other relevant content can be accessed on the online Focus site — enjoy!

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