means both one thing and its opposite ought not to be a stable tool for communication, since it would be an unreliable indicator of its utterer's intention.

It may be that appearances here are deceptive. In the case just described, the gestures might have a single, perhaps more general meaning than is revealed by the range of its ASOs — for example, "Move!". Precisely how the addressee should move would need to be inferred not just from the gesture but from further contextual elements too, like the nature of social interaction in which the gesture was produced (for example, friendly *versus* antagonistic interactions). In other cases, social relationships may determine which responses are satisfactory. For example, the 'reach' gesture is used to solicit climbing, proximity, or closer contact. It may be that the gesture is really used as a general request for physical contact (analogous to "Hold me!") that is satisfied differently depending upon the individuals involved. Such a request might be satisfied by climbing from an infant, but by a gentle touch from an adult male.

With more exhaustive analysis of the context of gesture production, ambiguities in the current lexicon might be identified and resolved. It may be that utterances of "Move!" are accompanied by facial expressions or vocalisations containing further information about the gesturer's intentions [11,12], or that satisfactory responses to contact solicitations vary with age and rank. Context-driven analysis of the variance between gestures and ASOs might therefore reveal more univocal intentions underlying different patterns of response. Alternatively, it might not support assignment to gestures of more precise meanings. Here we might conclude that gestures are only general attention-soliciting devices, with meanings analogous to "Hey!" or "Oi!" — as others have supposed [4,7].

The gestural lexicon outlined by Hobaiter and Byrne [2] is a huge achievement for primate science. It provides the most detailed answer yet given to Davidson's question with respect to our nearest living relatives, and the refinements suggested here would not be possible without the valuable dataset presented. At the same time, radical interpretation can be a momentous project, and the process of interpreting chimpanzee minds will not be accomplished quickly. Research into the context-variant elements of great ape gestural communication will be especially valuable in the completion of this task.

References

1. Davidson, D. (1973). Radical interpretation. Dialectica *27*, 314–328.
2. Hobaiter, C., and Byrne, R.W. (2014). The meanings of chimpanzee gestures. Curr. Biol. *24*, 1596–1600.
3. Genty, E., and Zuberbühler, K. (2014). Spatial reference in a bonobo gesture. Curr. Biol. *24*, 1601–1605.
4. Call, J., and Tomasello, M., eds. The Gestural Communication of Apes and Monkeys (Manhaw, NJ: LEA).
5. Grice, H.P. (1957). Meaning. Philosophic. Rev. *66*, 377–388.
6. Donald, M. (1991). Origins of the Modern Mind: Three Stages in the Evolution of Culture and Cognition (Cambridge, MA: Harvard University Press).
7. Tomasello, M. (2008). Origins of Human Communication (Cambridge, MA: MIT Press).
8. Moore, R. (2013). Imitation and conventional communication. Biol. Philosoph. *28*, 481–500.
9. Genty, E., Breuer, T., Hobaiter, C., and Byrne, R.W. (2009). Gestural communication of the gorilla (Gorilla gorilla): repertoire, intentionality and possible origins. Anim. Cogn. *12*, 527–546.
10. Cartmill, E., and Byrne, R.W. (2010). Semantics of primate gestures: intentional meaning of orangutan gestures. Anim. Cogn. *13*, 793–804.
11. Moore, R. (2013). Evidence and interpretation in great ape gestural communication. Humana Mente *24*, 27–51.
12. Liebal, K., Waller, B., Burrows, M., and Slocombe, K. (2013). Primate Communication: A Multimodal Approach (Cambridge: Cambridge University Press).

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Docking Interactions: Cell-Cycle Regulation and Beyond

In budding yeast, the mating pathway activates Far1 to inhibit G1 cyclins in complex with the cyclin-dependent kinase (Cln–Cdk). Yet, the molecular mechanism has remained largely unclear for over 20 years. A recent report helps shed light on this regulation.

Mardo Kõivomägi and Jan M. Skotheim*

Progression through the cell cycle is controlled by cyclin-dependent kinases (Cdk) in complex with cyclin regulatory subunits. Cyclins accumulate in distinct cell-cycle phases to drive specific events. To a first approximation, cyclin activity increases as the cell progresses through the cell cycle until plummeting in anaphase upon activation of the APC E3 ubiquitin ligase, which targets many cyclins for destruction. Interestingly, the cell cycles of fission yeast and frog embryo extracts can be driven by a single, highly active mitotic cyclin [1,2]. In these single cyclin models, it is presumed that distinct cell-cycle events are initiated at specific Cdk activity thresholds. However, all organisms whose cell cycles have been investigated have many cyclins, which must have important functions since they have not been lost through neutral mutation.

The importance of cyclin specificity for cell-cycle control was first revealed by genetic studies [3]. For example, the S-phase cyclins in yeast and animals, Clb5 and cyclin A, respectively, use a hydrophobic patch to dock substrates and target Cdk activity to initiate DNA replication [4]. It is now appreciated that all early cyclins in yeast likely have docking sites to recognize specific partners. This increased specificity compensates for the fact that the early cyclin–Cdk complexes are less active when examined on model substrates such as histone H1 peptide. This new quantitative model, based mostly on *in vitro* biochemistry, proposes that there is a handoff from more specific, but less active kinase complexes to less specific, but more

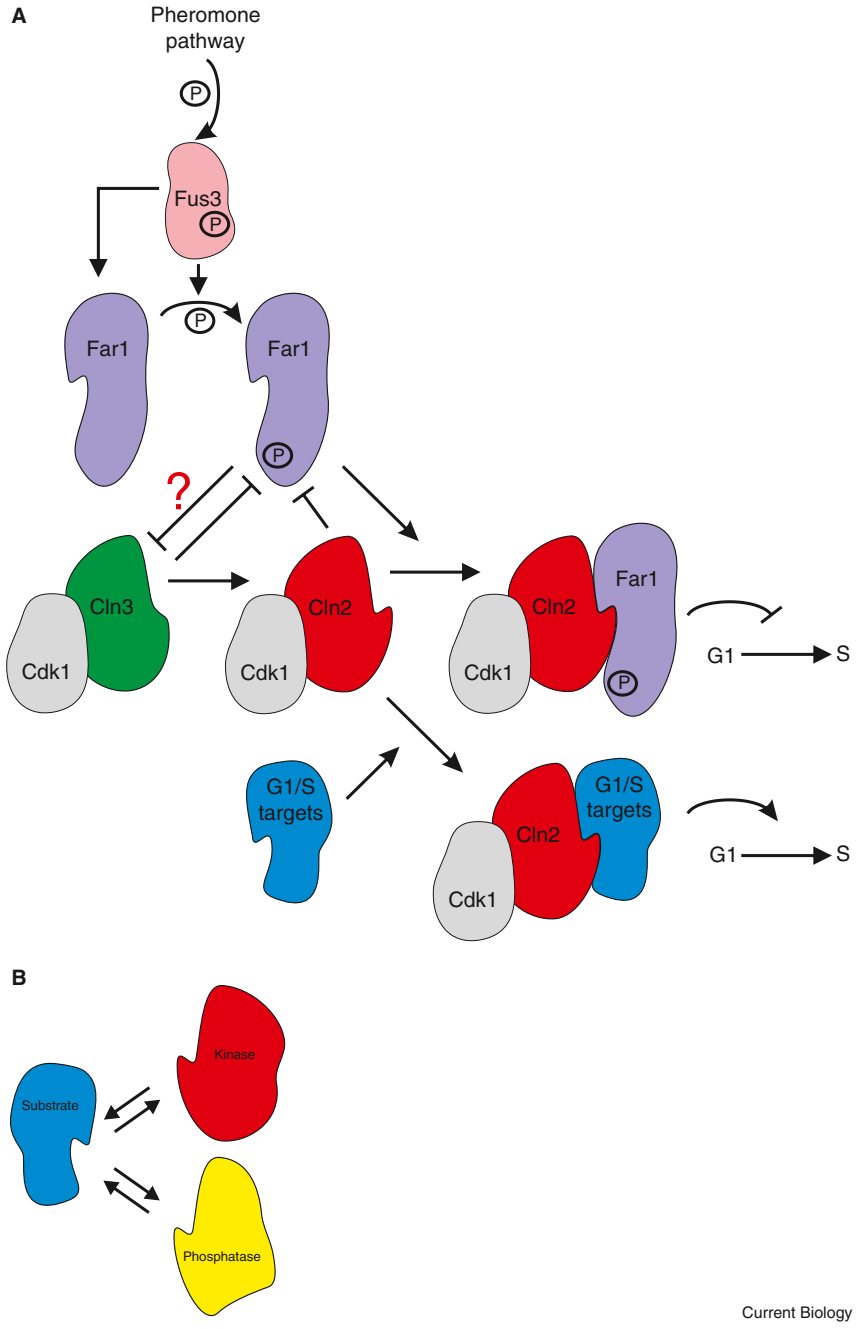

Figure 1. Pheromone signalling and overlapping docking interactions.

(A) The mating pheromone signal is transmitted through a MAP kinase cascade leading to the phosphorylation and activation of the MAPK Fus3. Activated Fus3 activates Far1 both by direct phosphorylation and by transcription. Phosphorylated Far1 arrests the cell cycle by inhibiting G1 cyclin complexes. (B) Competition between a kinase and a phosphatase for the same docking site may enhance switch-like transitions of the substrate's phospho-state.

active complexes with cell-cycle progression [5].

In a recent study in *Current Biology*, Pope *et al.* [6] are able to directly test the new quantitative model for cell-cycle progression *in vivo*. Native substrate recognition is bypassed by expressing cyclin and substrate fusion proteins attached to leucine zippers. These leucine zippers bind together to rewire the cyclin substrate docking network [7]. Using this system, it is possible to dock any cyclin–Cdk complex with any substrate so that the intrinsic activity of the complex can be assayed *in vivo*. Consistent with the new quantitative model [5], the earliest G1 cyclin Cln3 is weaker than its later cousin Cln2 and the S-phase cyclin Clb5, which, in turn, are weaker than the mitotic cyclin Clb2. The earlier the cyclin, the weaker the activity. Thus, high specificity and weak activity of early cyclins is likely to prevent premature phosphorylation of later targets.

The reliance of early low-activity cyclin–Cdk complexes on docking mechanisms might be exploited by Cdk inhibitors. While it was initially thought that Far1 functioned through inhibiting kinase activity [8], this conclusion was subsequently challenged [9]. Now, Pope *et al.* [6] show that Far1 inhibits Cln–Cdk complexes by competing out their targets (Figure 1A). Increasing Far1 decreases the interaction between Cln2–Cdk complexes with two of their endogenous targets, Whi5 and Sic1. A time course synchronously releasing cells from mitosis showed that there was a sufficient amount of Far1 to inhibit all the Cln2 prior to *Start*, the point of commitment to cell division [10]. Thus, activated Far1 may serve as a competitive stoichiometric inhibitor of Cln–Cdk complexes, while a mystery remains as to how the pheromone-dependent phosphorylation on T306 of Far1 serves to activate its inhibitory function. This study represents an important step forward because it develops an *in vivo* system to examine the Far1 inhibition mechanism, which has remained so elusive for over 20 years.

An additional complexity revealed by Pope *et al.* [6] is that the mechanism of inhibition of the upstream cyclin Cln3 may be different from that for Cln2 because its docking site is likely different. The potentially different biochemical mechanisms underlying G1 cyclin inhibition may be reflected *in vivo*, where moderate pheromone concentrations completely inhibit Cln1 and Cln2, but not Cln3 [11]. Elucidation of the more complex mechanisms underlying Far1 activation and mechanism of inhibition of the entire G1 cyclin family will likely require more quantitative *in vitro* investigation.

Just as docking interactions can be used by cyclin–Cdk complexes to determine their targets and order events in the cell cycle, such interactions may also be employed

by the counteracting phosphatases (Figure 1B). While phosphatase docking is much less studied, recent work suggests it may be prevalent and, intriguingly, overlap with kinase docking. The protein phosphatase 1 docking site on the retinoblastoma protein overlaps with the known docking site for S phase cyclin–Cdk [12]. A new study examining Ca^{2+}/calmodulin-regulated phosphatase (CN) showed that its docking specificity overlaps with that of the pheromone-activated MAPK Fus3 [13]. This presents two examples where competing kinase–phosphatase pairs recognize the same docking site, which might enhance switch-like transitions of the phospho-state of individual targets. In addition, we are immediately provided with a mechanism through which competition between kinase–phosphatase pairs can be conserved. Goldman *et al.* [13] compared kinase and CN targets in mammals and yeast to find that while nearly no specific substrates were conserved, the same kinases opposed CN on both sets of substrates. To evolve co-regulation of a substrate by a specific kinase–phosphatase pair with overlapping docking specificity, mutation only needs to generate a single docking site, rather than two. Thus, overlapping docking specificity may explain why the same network functions are regulated by the same kinases and phosphatases across diverse eukaryotes.

References

1. Coudreuse, D., and Nurse, P. (2010). Driving the cell cycle with a minimal CDK control network. Nature *468*, 1074–1079.
2. Murray, A.W., and Kirschner, M.W. (1989). Cyclin synthesis drives the early embryonic cell cycle. Nature *339*, 275–280.
3. Bloom, J., and Cross, F.R. (2007). Multiple levels of cyclin specificity in cell-cycle control. Nat. Rev. Mol. Cell Biol. *8*, 149–160.
4. Wilmes, G.M., Archambault, V., Austin, R.J., Jacobson, M.D., Bell, S.P., and Cross, F.R. (2004). Interaction of the S-phase cyclin Clb5 with an "RXL" docking sequence in the initiator protein Orc6 provides an origin-localized replication control switch. Genes Dev. *18*, 981–991.
5. Kõivomägi, M., Valk, E., Venta, R., Iofik, A., Lepiku, M., Morgan, D.O., and Loog, M. (2011). Dynamics of Cdk1 substrate specificity during the cell cycle. Mol. Cell *42*, 610–623.
6. Pope, P.A., Bhaduri, S., and Pryciak, P.M. (2014). Regulation of cyclin-substrate docking by a G1 arrest signaling pathway and the Cdk inhibiitor Far1. Curr. Biol. *24*, 1390–1396.
7. Bashor, C.J., Helman, N.C., Yan, S., and Lim, W.A. (2008). Using engineered scaffold interactions to reshape MAP kinase pathway signaling dynamics. Science *319*, 1539–1543.
8. Peter, M., and Herskowitz, I. (1994). Direct inhibition of the yeast cyclin-dependent kinase Cdc28-Cln by Far1. Science *265*, 1228–1231.
9. Gartner, A., Jovanović, A., Jeoung, D.I., Bourlat, S., Cross, F.R., and Ammerer, G. (1998). Pheromone-dependent G1 cell cycle arrest requires Far1 phosphorylation, but may not involve inhibition of Cdc28-Cln2 kinase, in vivo. Mol. Cell Biol. *18*, 3681–3691.
10. Doncic, A., Falleur-Fettig, M., and Skotheim, J.M. (2011). Distinct interactions select and maintain a specific cell fate. Mol. Cell. *43*, 528–539.
11. Doncic, A., and Skotheim, J.M. (2013). Feedforward regulation ensures stability and rapid reversibility of a cellular state. Mol. Cell. *50*, 856–868.
12. Hirschi, A., Cecchini, M., Steinhardt, R.C., Schamber, M.R., Dick, F.A., and Rubin, S.M. (2010). An overlapping kinase and phosphatase docking site regulates activity of the retinoblastoma protein. Nat. Struct. Mol. Biol. *17*, 1051–1057.
13. Goldman, A., Roy, J., Bodenmiller, B., Wanka, S., Landry, C.R., Aebersold, R., and Cyert, M.S. (2014). The calcineurin signaling networks evolves via conserved kinase-phosphatase modules that transcend substrate identity. Mol. Cell. http://dx.doi.org/10.1016/j.molcel.2014.05.012.

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Coevolution: Puff Pollination in Tropical Flowers

A new study shows that birds plucking anthers of the Melastome, *Axinaea*, demonstrate a novel bird pollination mechanism. Each stamen of *Axinaea* offers a nutrient-rich, berry-like food body that, when bitten, releases a puff of pollen allowing transfer to stigmas by wind or the pollen-dusted bird.

Joan Edwards

Flowers and their pollinators offer a palette of diversity to study coevolution and provide data for unraveling Darwin's "abominable mystery", the sudden appearance and extraordinarily rapid diversification of the angiosperms [1]. Yet with over 350,000 species of flowering plants [2], we are still discovering new methods of pollination. For New World bird pollination syndromes we typically think of tubular red flowers, copious amounts of dilute nectar, and the whirr of hummingbirds hovering as they collect nectar through specially engineered tongues [3,4]. Not so for the novel bird pollination system reported for the neotropical Melastomataceae, *Axinaea*, by Dellinger *et al.* in this issue of Current Biology [5], adding a new twist to our thinking about how birds can effect pollination and how pollination syndromes can develop.

For *Axinaea* flowers, the bird pollinators are not hummingbirds, but a diverse group of tropical fruit-eating tanagers. Flowers vary in color from white to pale lavender to red and offer no nectar reward, but instead provide berry-like food bodies rich in citric acid, fructose and glucose (Figure 1A). In return for the food bodies, the birds power a uniquely designed bellows pollination system, where the bite of the bird's beak releases a puff of pollen that is either carried by wind or by pollen-dusted birds depositing pollen on the exerted stigmas of the next flowers they visit.

The authors document this system with detailed analyses of stamen morphology. Using X-ray computed tomography, SEM and thin sectioning, they present stunning 3-D images and longitudinal cross-sections illustrating the anatomy of the anthers. Each of the ten anthers in the flower is modified to be a miniature turkey baster where the 'bulb' is the nutritious food body made up of large air-filled cells that connects to the 'shaft' made of pollen-filled anther sacs with a pore-sized opening at the end. The whole operation points downward to the center of the flower, so that when the bird plucks the food body, it forces air from the food body into the anther sacs and releases a pollen puff that is directed towards the top of the flower and the bird's head and beak (Figure 1B).