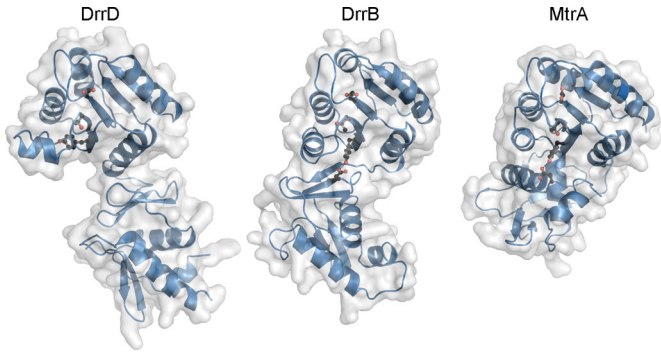
Papers of the Week

Influence of Interdomain Interfaces ♦

♦ See referenced article, *J. Biol. Chem.* 2010, **285,** 32325–32335

Regulation of Response Regulator Autophosphorylation through Interdomain Contacts



Ribbon structures of response regulator proteins DrrD, DrrB, and MtrA; surfaces, shown in *white*, illustrate differences in the extent of interdomain interfaces, which correlate with the protein's readiness for autophosphorylation.

Two-component systems are simplified stimulus-response regulatory networks typically involving a sensory histidine kinase that activates DNA-binding response regulator (RR) proteins via phosphorylation of their receiver domains. However, studies seem to indicate that not all RR proteins are equal in any given state (active or inactive), as inter- or intramolecular interactions between the receiver and DNA-binding domains can bias conformational equilibria by favoring one state over another. In this Paper of the Week, Christopher Barbieri and colleagues examined the effect of these interdomain interfaces by determining the phosphorylation rates of five RRs of the bacterial OmpR/PhoB family, either in full or just the isolated receiver domains. They identified a strong correlation between the size of interdomain interfaces in the inactive state (determined through structural analysis) and ease of autophosphorylation; readily phosphorylatable proteins had smaller interfaces. Such differences in autophosphorylation were not observed in the isolated receiver domains or in phosphorylation catalyzed by histidine kinases, suggesting these interfaces serve to limit phosphorylation by other potential substrates like acetyl phosphate and maintain signal specificity in two-component systems.

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