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Surveying non-visual arrestins reveals allosteric interactions between functional sites

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Abstract

Arrestins are important scaffolding proteins that are expressed in all vertebrate animals. They regulate cell signaling events upon binding to active G-protein coupled receptors (**GPCR**) and trigger endocytosis of active GPCRs. While many of the functional sites on arrestins have been characterized, the question of how these sites interact is unanswered. We used anisotropic network modelling (**ANM**) together with our covariance compliment techniques to survey all of the available structures of the non-visual arrestins to map how structural changes and protein-binding affect their structural dynamics. We found that activation and clathrin binding have a marked effect on arrestin dynamics, and that these dynamics changes are localized to a small number of distant functional sites. These sites include α-helix 1, the lariat loop, nuclear localization domain, and the C-domain β-sheets on the C-loop side. Our techniques suggest that clathrin binding and/or GPCR activation of arrestin perturb the dynamics of these sites independent of structural changes.

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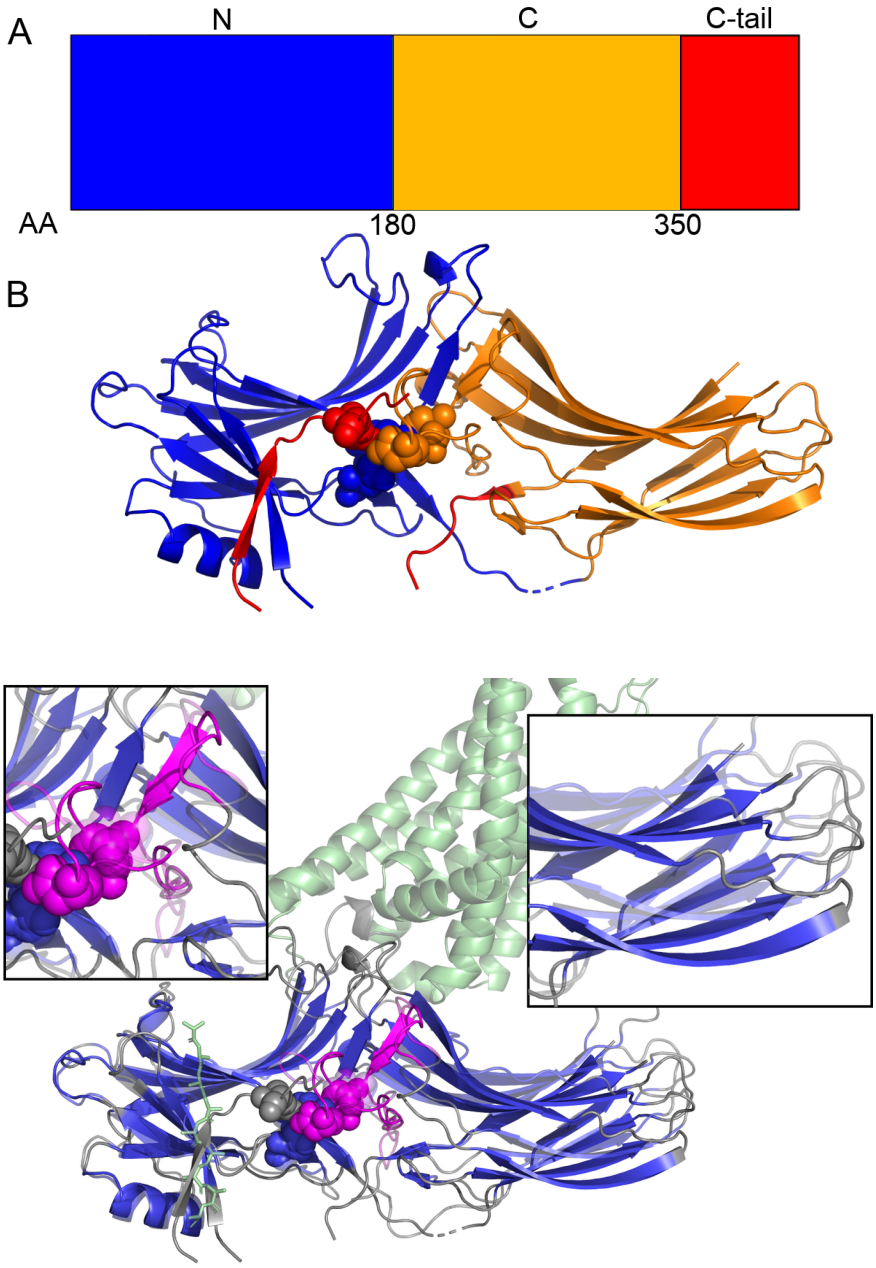

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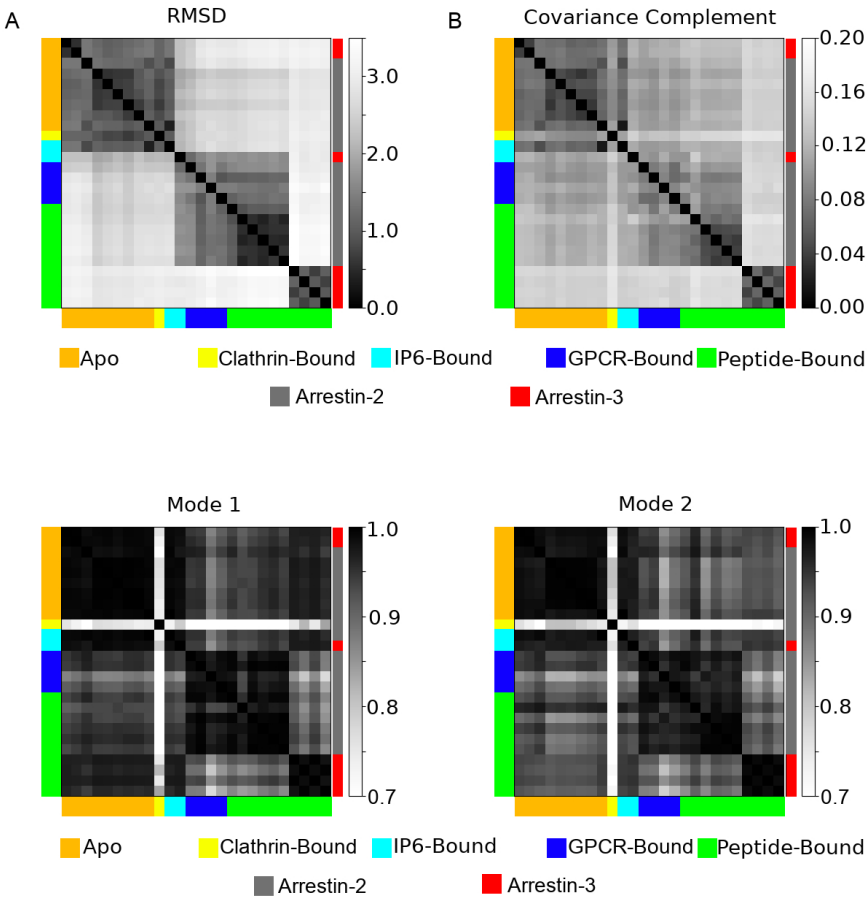

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