

# Intrinsically disordered region of talin's FERM domain functions as an initial PIP<sub>2</sub> recognition site

Jannik Buhr<sup>1,2</sup> ([jannik.buhr@h-its.org](mailto:jannik.buhr@h-its.org), [jmbuhr.de](https://orcid.org/0000-0002-9300-0000)), Florian Franz<sup>1,2</sup>, Frauke Gräter<sup>1,2</sup>

1. Heidelberg Institute for Theoretical Studies (HITS)  
2. Heidelberg University

## Abstract

Focal adhesions mediate the interaction of the cytoskeleton with the extracellular matrix (ECM). Talin is a central regulator and adaptorprotein of the multiprotein focal adhesion complexes and is responsible for integrin activation and force-sensing. We evaluated direct interactions of talin with the membrane lipid phosphatidylinositol 4,5-bisphosphate (PIP<sub>2</sub>) by means of molecular dynamics simulations. A newly published autoinhibitory structure of talin, where common PIP<sub>2</sub> interaction sites are covered up, sparked our curiosity for a hitherto less examined loop as a potential site of first contact. We show that this unstructured loop in the F1 subdomain of the talin1 FERM domain is able to interact with PIP<sub>2</sub> and can facilitate further interactions by serving as a flexible membrane anchor.

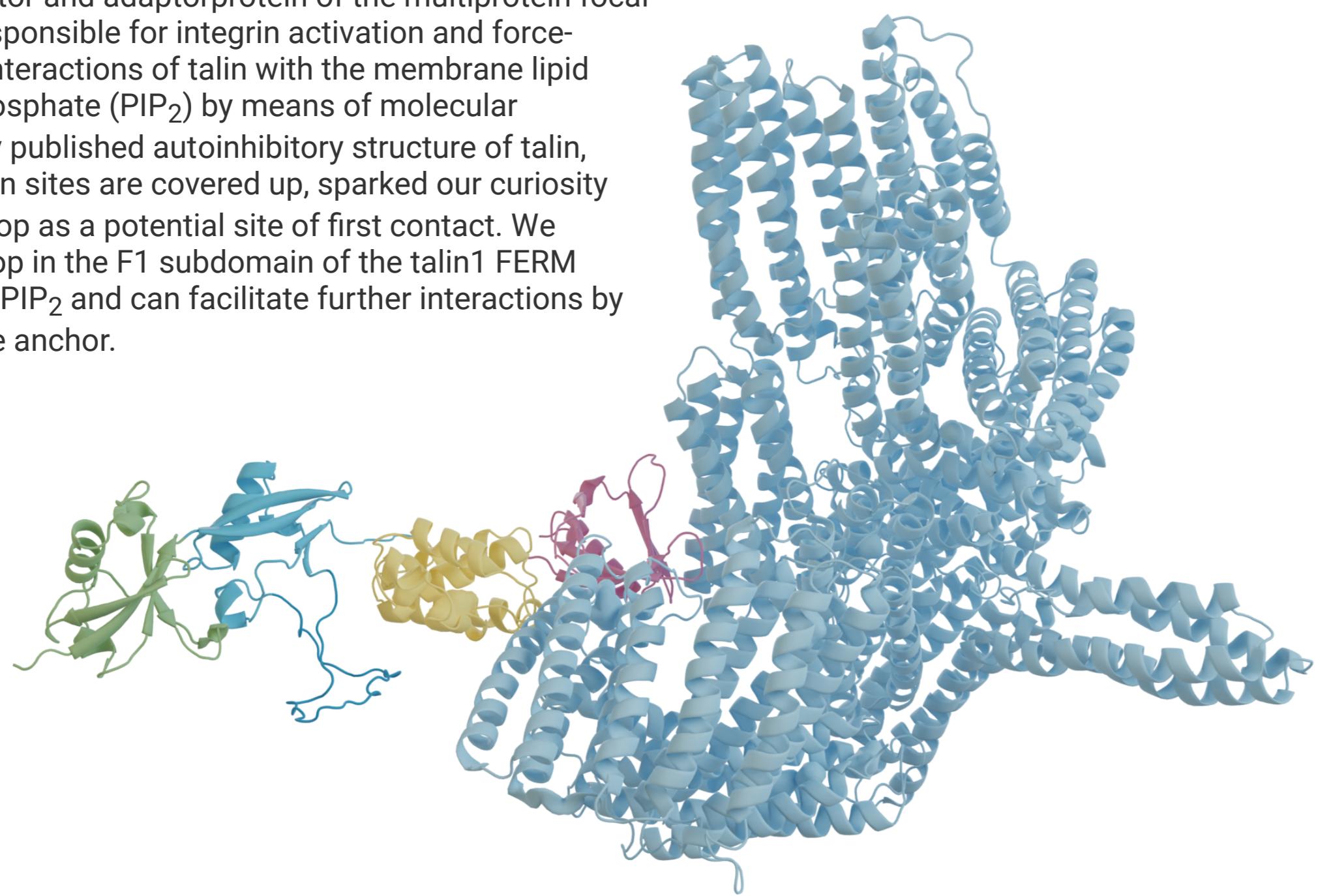


Figure 1: The autoinhibited (Cryo-EM) structure of Talin1 found by Dedden et al. (2019) aligned with the structure of the FERM domain by Elliott et al. (2010) and the modelled flexible loop in F1 (darker cyan)

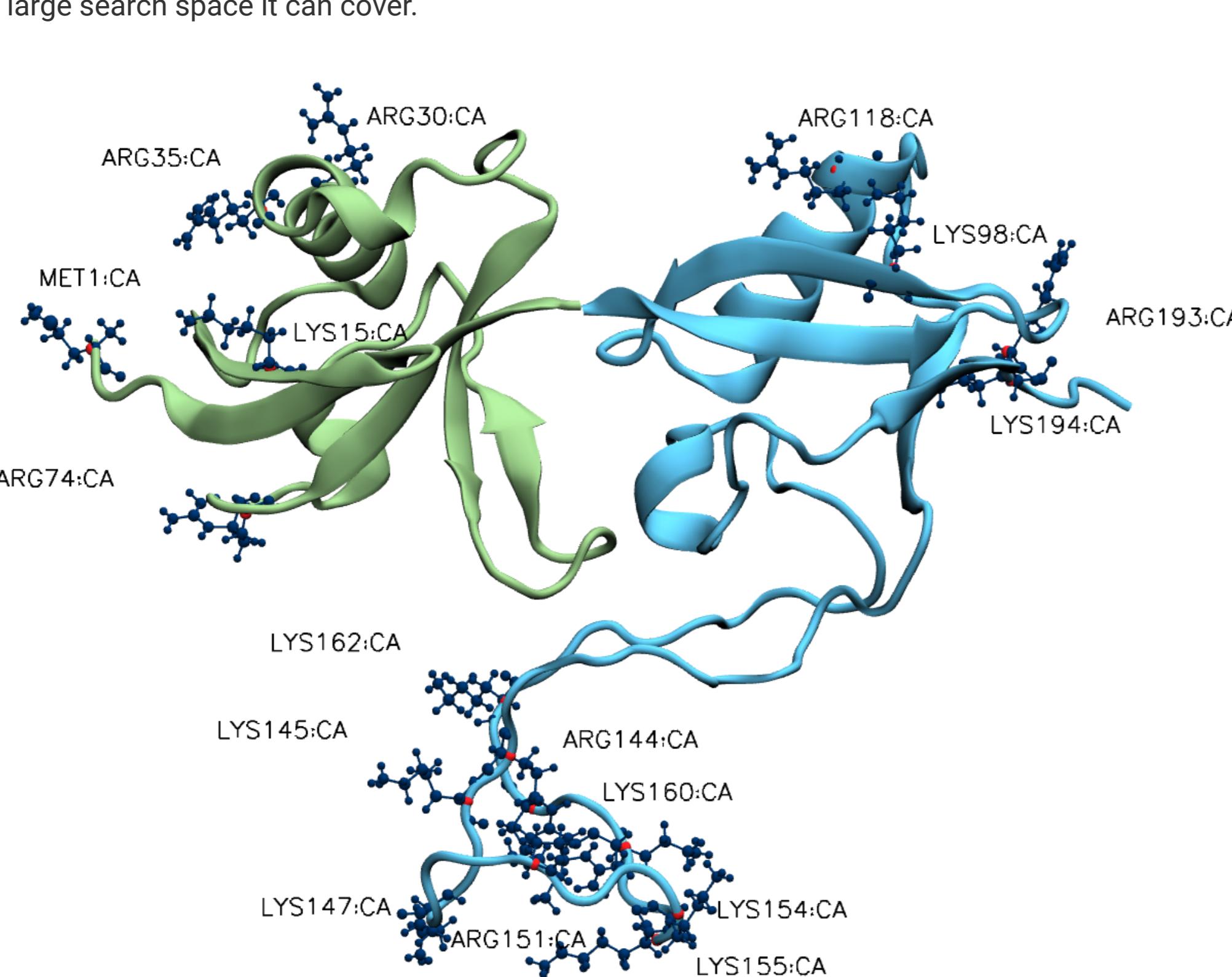
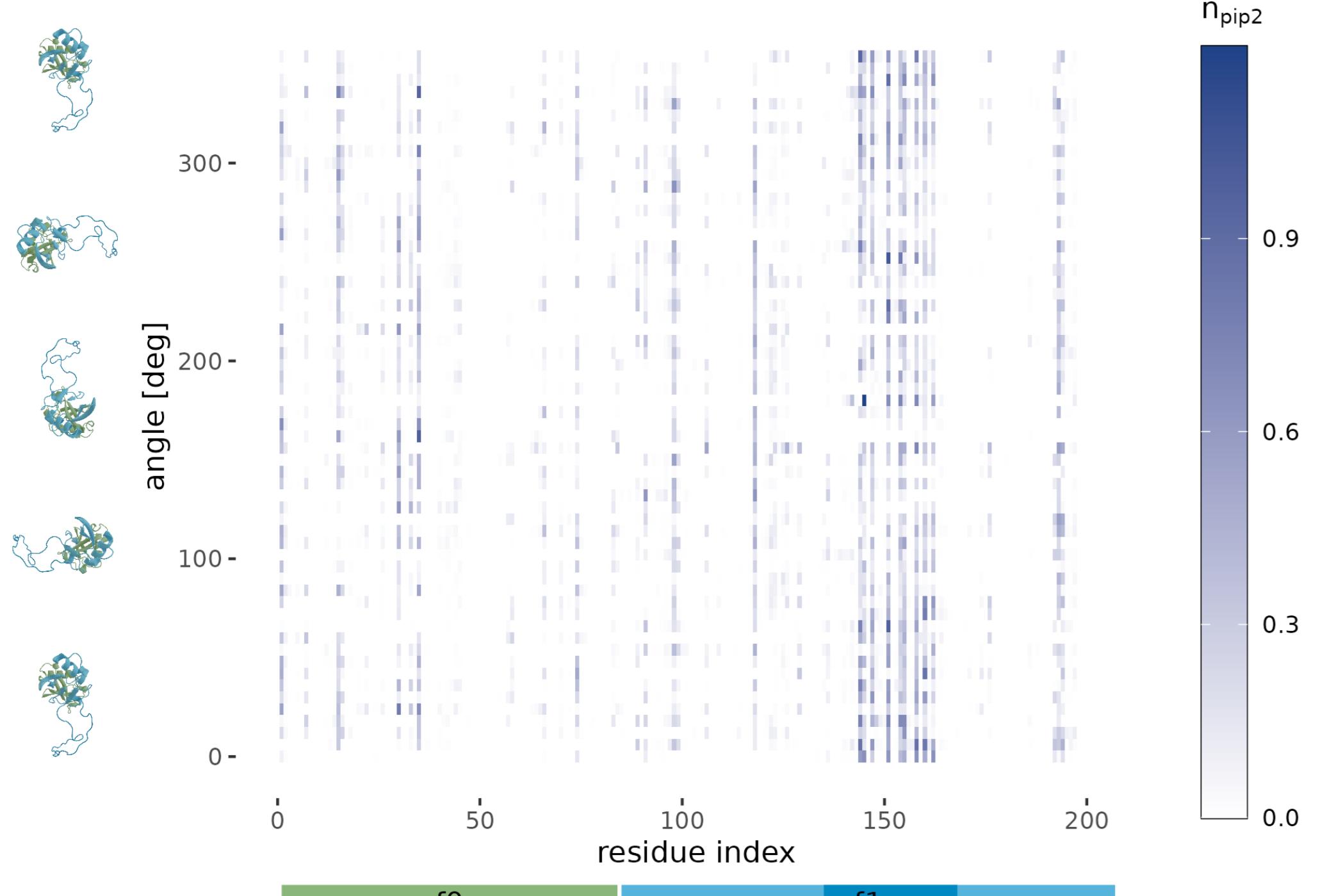
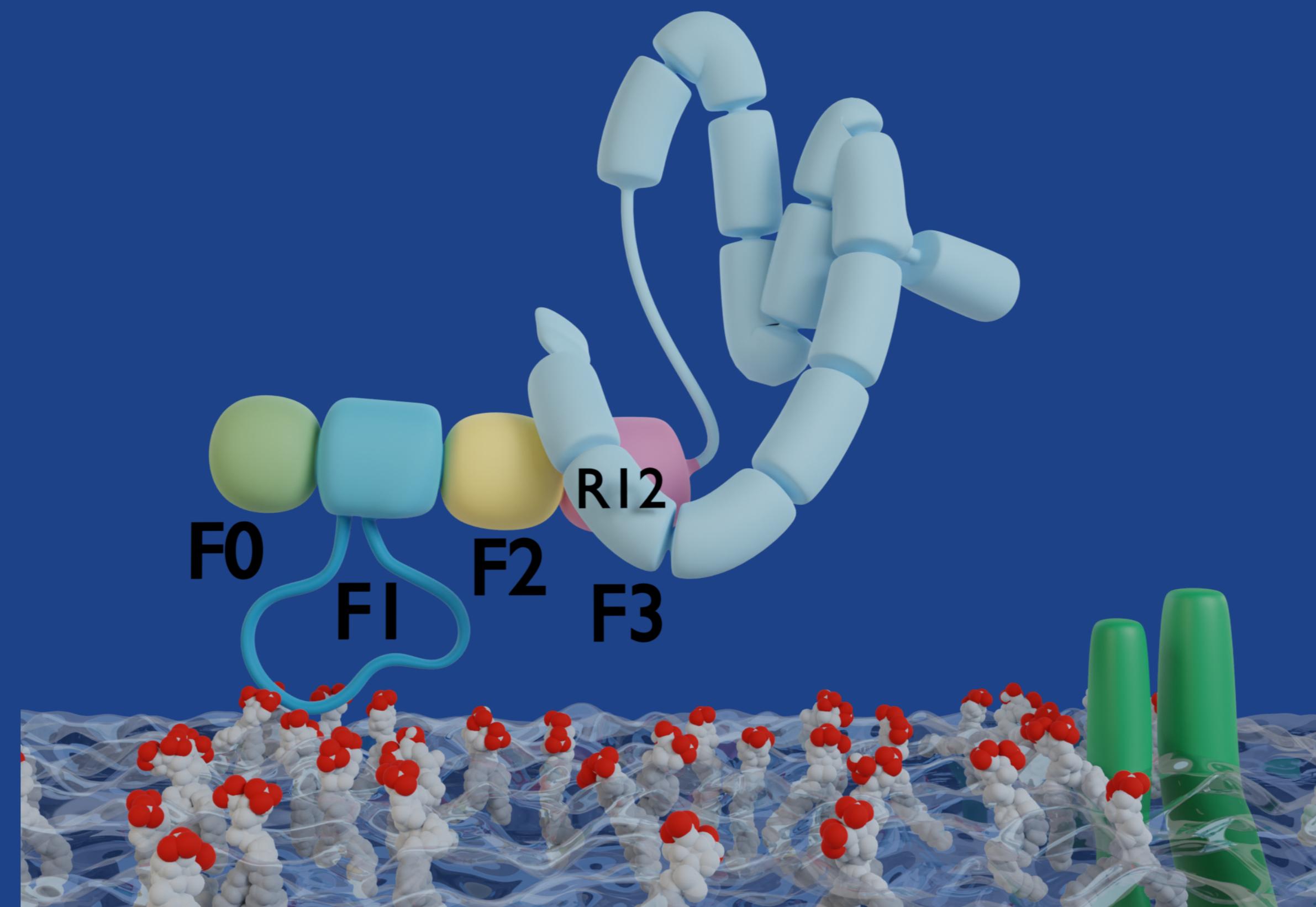


Figure 3: The residues of F0F1 interacting with PIP<sub>2</sub> are highlighted in blue, with their CA-atoms labelled

# Unstructured loop of Talin's FERM domain can serve as a flexible membrane anchor

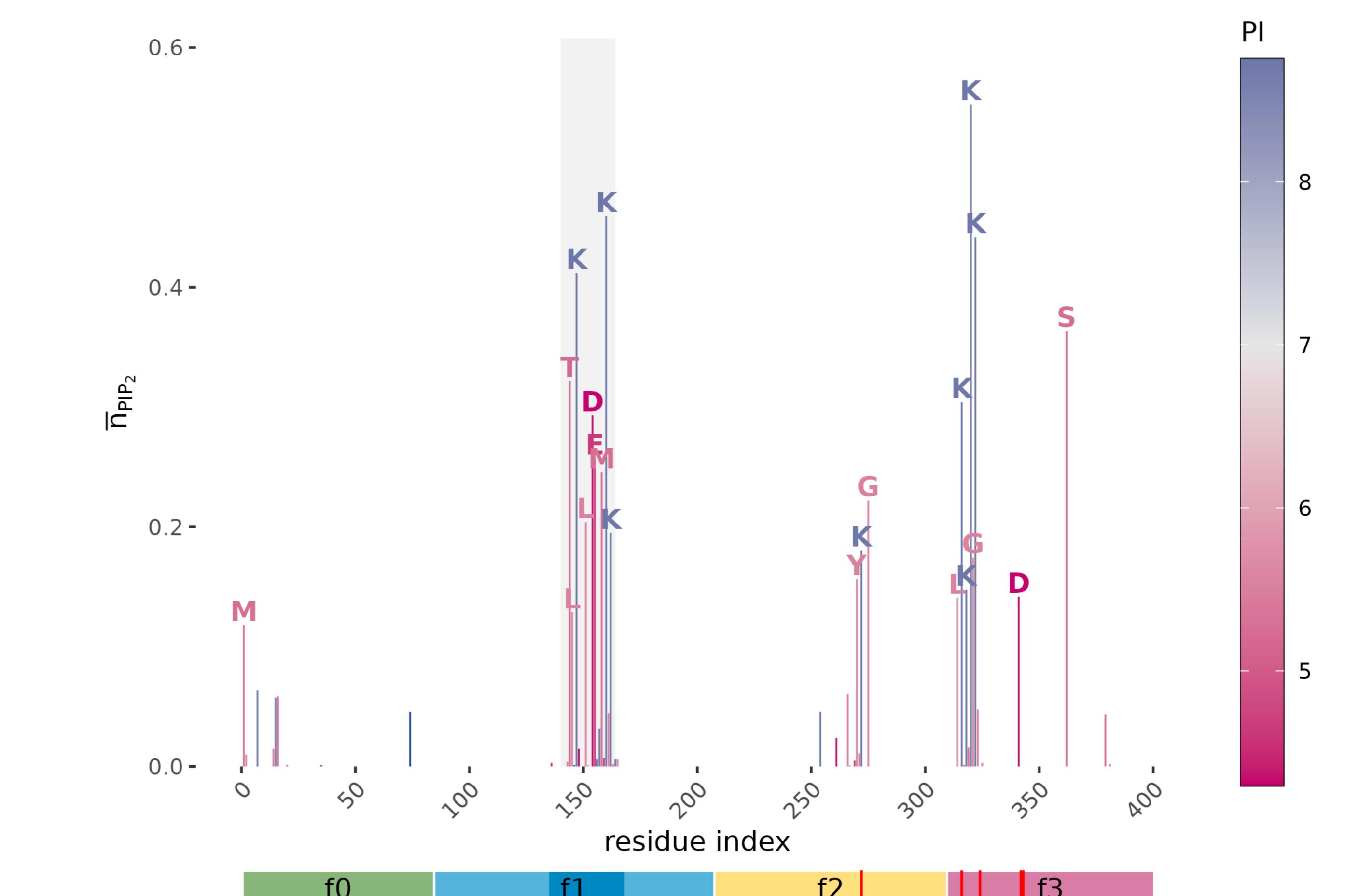
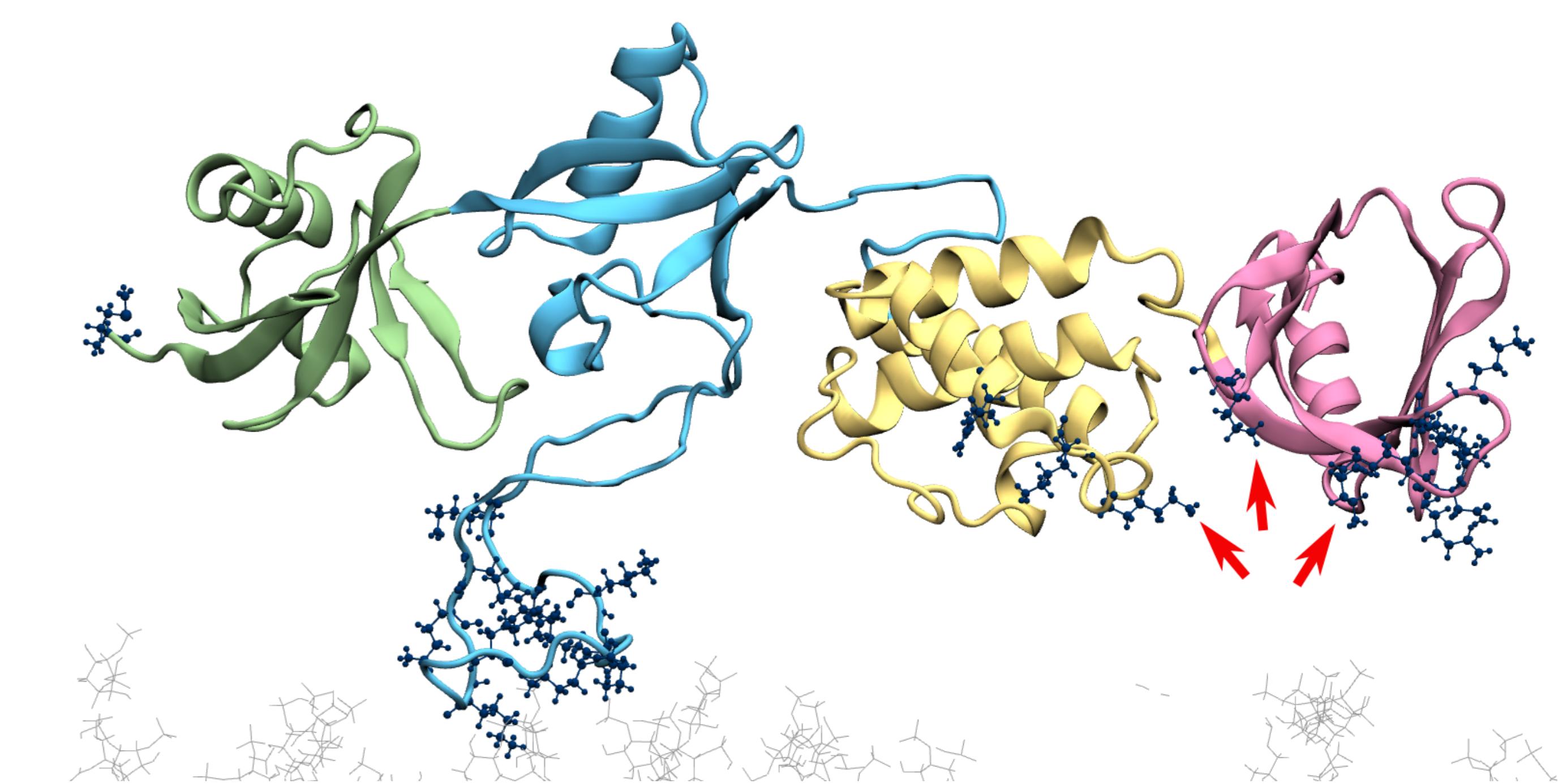
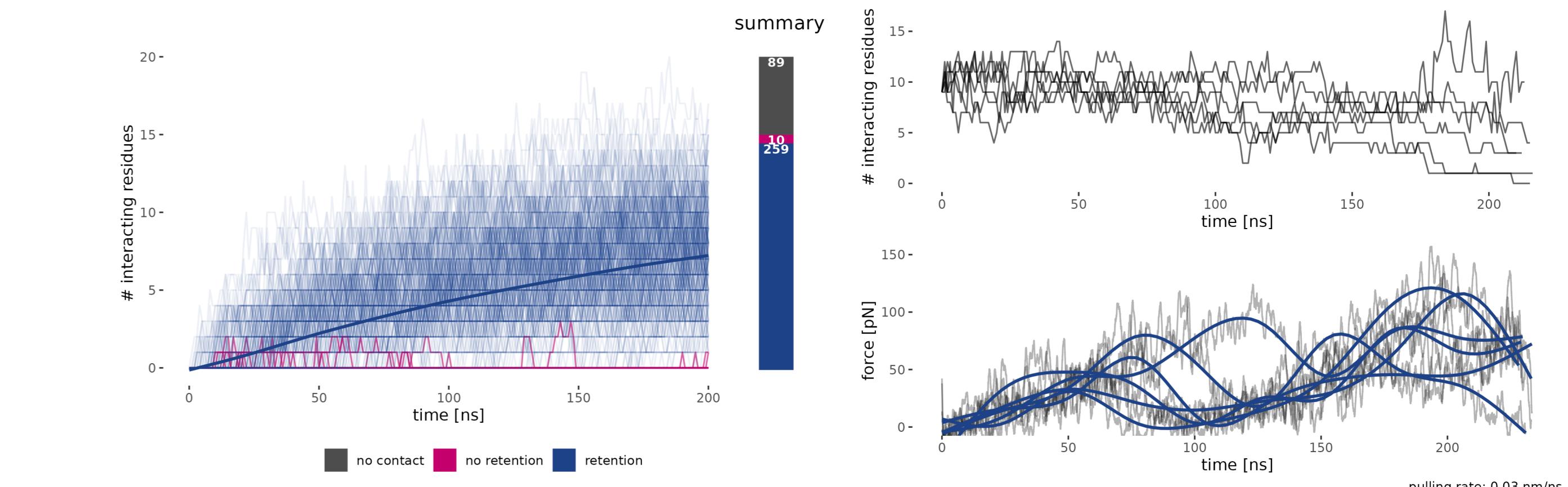
This allows for interaction with PIP<sub>2</sub> even in Talin's autoinhibited form and paves the way to establish known binding surfaces.



Follow the QR code or visit <https://github.com/hits-mbm-dev/paper-talin-loop> for the repository of the paper draft. Or even better yet, talk to me in front of the poster!



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