

DATE: Day ____ Month ____ Year 2025

SUMMARY of FY2024 RESEARCH RESULTS REPORT For International Collaborative Research with IPR, Osaka University

Research Title		Computational investigation of dynamically coupled interfaces in bHLH -PAS domain transcription factors
Applicant	Name	Ashutosh Srivastava
	Affiliation	INDIAN INSTITUTE OF TECHNOLOGY GANDHINAGAR
	Present Title	Computational investigation of dynamically coupled interfaces in bHLH -PAS domain transcription factors
Research Collaborator (Host PI)		Tiwari Sandhya Premnath

Summary

Understanding how proteins dynamically interact to form functional complexes remains a key challenge in structural biology. This project focused on bHLH-PAS domain-containing transcription factors—key regulators of circadian rhythms, neuronal development, and stress responses—which form heterodimers through context-dependent PAS domain interactions. While individual structures are known, the mechanistic basis of their dimerization and dynamic coupling remains unclear.

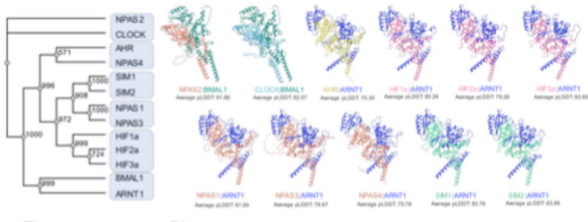


Figure 1 - Phylogenetic tree illustrating the evolutionary relationships among bHLH-PAS transcription factors and the cartoon representation of the modeled complexes with corresponding average pLDDT values from AlphaFold3.

Using a combination of AlphaFold3-predicted models, molecular dynamics simulations, and an elastic network model-based approach developed in Assoc. Prof. Tiwari's lab, we studied 13 heterodimeric complexes (Figure 1). Our analysis revealed that intrinsic dynamic coupling across PAS domains differs by interface type (PAS-A vs. PAS-B) and complex class, despite high structural conservation. Notably, dynamics captured through normal mode analysis provided greater insight into complex-specific behavior than sequence or structure alone.

These findings have been compiled into a manuscript, currently under review at *Biophysical Journal* and available soon on bioRxiv. This collaboration forms a key part of Karthik Sudarsanam's PhD research, and further investigations into functional implications of dynamic coupling are planned.

- *Deadline: May 9, 2025
- *Please submit it to E-mail: tanpakuken-kyoten@office.osaka-u.ac.jp.
- *Please describe this summary within 1 sheet. Please DON'T add some sheets.
- *This summary will be published on the web.