Track & trace transcription factors through truncations

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Transcription factors (TFs) bind to motif sequences in regulatory regions near target genes to control their transcription. Live-cell imaging studies have revealed that binding to target sequences is highly dynamic. However, since in most previous imaging studies the position of target genes was unknown, it is not well understood how different TF domains contribute to the TF binding dynamics at specific target locations. In addition, TFs are localized in clusters of high local concentrations, and it is unclear how these clusters affect the dynamic binding of single TF molecules.

In this project, we aim to understand how different domains of the well-studied yeast TF Gal4 contribute to its target search and binding dynamics. Our lab recently developed a method to measure live-cell TF binding dynamics at a single locus of interest (Pomp et al., bioRxiv, 2023). We will combine this method with various Gal4 truncation mutants (Meeussen et al., NAR, 2023) to study the binding dynamics of these mutants at a target gene. This will allow us to answer questions such as; which domains contribute to long specific binding and the TF binding frequency at the target gene? How does TF clustering affect the TF residence time? How does cooperativity affect binding dynamics? Does the chromatin state influence TF binding dynamics? All together, these answers will reveal fundamental principles of how TF target search and TF binding dynamics at the target gene are regulated.

References

Pomp, W., Meeussen J.V.W. and Lenstra, T.L., (2023) Transcription factor exchange enables prolonged transcriptional bursts. bioRxiv: 2023.05.15.540758

Meeussen, J.V.W., Pomp, W., Brouwer, I., de Jonge, W.J., Patel, H.P. and Lenstra, T.L. (2023) Transcription factor clusters enable target search but do not contribute to target gene activation. NAR: gkad227