

## Unravelling the organization of bacterial chromatin

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The bacterial genome is folded and compacted into a body referred to as the nucleoid due to the activity of nucleoid-associated proteins (NAP's). As a consequence of their role in global genome organization these proteins also act as pleiotropic regulators of transcription. One of the key players in these processes is H-NS. This is an abundant, multimeric protein with a binding preference for A/T rich regions along the genome. Its binding to these regions is associated with transcriptional silencing and has been suggested to be a mechanism to specifically target and silence newly acquired foreign DNA and protect the host against its potentially harmful effects.

A lot of progress in the understanding of H-NS action has been booked in recent years. Our main aim has been to establish the structure, kinetics, mode of binding and the role of H-NS in global genome organization. To this purpose we used a combination of scanning force microscopy imaging, single-molecule micromanipulation and theoretical modeling of H-NS-DNA complexes. Initially, we demonstrated that H-NS organizes DNA by bridging two DNA duplexes and put forward evidence that this mode of binding is also key to the role of H-NS as repressor. In recent follow up studies, we showed that H-NS acts as a dimer, that H-NS dimers are stacked side-by-side between bridged duplexes and determined the dimensions of the dimer. Moreover, we determined the binding kinetics of *individual* H-NS dimers and the forces required to open up H-NS-bridged regions. Finally, combining the *in vitro* structural observations and *in vivo* ChIP-on-chip data for binding of H-NS along the genome, we can now explain the higher order organization of the genome in the long known topologically isolated domains.