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Talk 1 and Talk 2:

Gene Regulation, Facilitated Diffusion, and Crowding (I, II)

The regulation of the genetic information stored in DNA is controlled by DNA binding proteins called transcription factors (TFs). TFs locate their designated binding site by using the naturally available "fuel" provided by their thermal environment. It was realised relatively early that the TFs do not simply diffuse three-dimensionally to locate their target site on the DNA. Rather, they perform facilitated diffusion [1], i.e., they utilise the topology of the DNA to enhance the efficiency of their search. The facilitated diffusion model will be introduced and recent evidence from single molecule experiments discussed. In particular, the role of the conformations of DNA will be addressed and shown that the search process is improved when the DNA is more coiled [2].

Apart from the TF location to the target site, it will be discussed how the expression of one gene controls another downstream gene, in particular, how the accuracy of this control can be effected [3]. The next step is then to take the above models, designed for dilute scenarios in typical in vitro experiments, to the more complex environment of living cells [4].

Finally, the crowded state of the cellular cytoplasm by large molecules will be addressed [5] and shown how aspects of the dynamics and the conformation of DNA are changed. Knowledge about these facts is important to understand how gene regulation works in living cells.

[1] PH v Hippel and O Berg, *J Biol Chem* 264, 675 (1989).

[2] B vd Broek, MA Lomholt, S-MJ Kalisch, R Metzler, and GJL Wuite, *Proc Natl Acad Sci USA* 105, 15738 (2008); MA Lomholt, B vd Broek, S.-M. J. Kalisch, GJL Wuite, and R Metzler, *Proc Natl Acad Sci USA* 106, 8204 (2009).

[3] O Pulkkinen and R Metzler, *Phys Rev Lett* 110, 198101 (2013).

[4] M Bauer and R Metzler, *PLoS ONE* 8, e53956 (2013).

[5] F Hoefling and T Franosch, *Rep Prog Phys* 76, 046602 (2013); E Barkai, Y Garini, and R Metzler, *Phys Today* 65(8), 29 (2012).