Transcription is the process in which RNA polymerase synthesizes messenger RNA during the readout of a gene on the DNA. This process is regulated by, amongst others, transcription factors. These are proteins that activate or repress transcription by binding to specific locations on the DNA, often near the promoter, which is the binding location of RNA polymerase. However, these proteins also bind to other parts of the DNA and thus, the total amount of DNA available for these proteins to bind to competes with the specific binding to promoter regions. [1]

Somewhat surprisingly, this ‘next level’ of transcription regulation has not been systematically addressed yet. Indeed, several processes in the cell are expected to lead to significant variations in the amount of accessible DNA to the proteins involved in transcription regulation. This affects the chemical potential of the proteins involved, which in turn influences the fraction of bound proteins to the promoter and operator regions, and thus the overall transcription rates. Such behavior follows from the basic statistical thermodynamics for simple genetic architectures. [2]

In this project we quantitatively investigate how non-specific DNA influences transcription, and expand the theoretical framework that predicts transcriptional behavior. To determine the effect of the number of non-specific base-pairs on the transcription rate, transcription rates will be monitored using a *Lac* operator in a simple repression architecture. A construct called Broccoli-DNA is used as a reporter gene, which is transcribed into mRNA aptamers that fluoresce upon binding to a small dye (DFHBI-1T). [3] This allows us to directly measure transcription *in vitro* in real time*.*

If successful, this work will pin down the regulatory role of the accessible genome size in biological cells and provide a next level of transcription regulation, that is, regulation beyond the direct interactions between operator regions and transcription factors.