The transcription activator NF-κB is a key player in the inflammatory response, and for this reason its deregulation can lead to a variety of inflammation-related diseases, including cancer. Live-cell imaging shows a rich variety of NF-κB nuclear localization dynamics in response to stimuli, including oscillations. Understanding the role of this dynamics in the processing of an external signal into the adequate transcriptional output can thus have important implications in physiological and pathological situations. To investigate this process, we used microfluidics and live cell imaging of GFP-NF-κB cells to characterize how NF-κB dynamics behaves under time-varying stimuli. We found that oscillations synchronize 1:1 to a wide variety of periodic inputs. In these synchronous conditions we found that NF-κB oscillations translate into different dynamical patterns of mRNA production, ranging from oscillating dynamics to slow accumulation of the transcript. Furthermore, we found that each dynamical pattern is enriched for genes related to different functions, highlighting the connection between dynamics and function in this system.

The next step is to understand how this dynamic control of transcription takes place at single-cell level, where gene expression is inherently stochastic. To address this, we have imaged living cells in an MS2 system allows the visualization of nascent transcription dynamics of a single gene under the control of NF-κB. We will discuss here our first insights on how NF-κB dynamics modulates stochasticity in the transcriptional response.