



Canadian Association
of Physicists

Association canadienne
des physiciens et physiciennes

Contribution ID: 3384 Type: **Oral Competition (Undergraduate Student) / Compétition orale (Étudiant(e) du 1er cycle)**

(U*) Can Confocal Microscopes Detect Transcriptional Condensates?

Wednesday, 8 June 2022 15:45 (15 minutes)

Recently, it has been proposed that gene transcription occurs in transcriptional condensates. Transcriptional condensates are membraneless nuclear compartments formed through liquid-liquid phase separation. These condensates create regions with a high concentration of transcription factors which could provide an environment for transient transcription factor binding to efficiently govern specific gene expression. The existence of transcriptional condensates, however, is not firmly established. The goal of this project was to predict whether condensates containing the Bicoid protein could be detected using a confocal microscope. Bicoid is a transcription factor in *Drosophila melanogaster* embryos which controls anterior-posterior patterning of the embryo. The project began by examining the structure of Bicoid with bioinformatic tools. It was found that Bicoid contains intrinsically disordered regions necessary for a protein to undergo liquid-liquid phase separation. Then confocal images of a nucleus containing a Bicoid condensate were simulated under varying physical and imaging parameters. These images were analyzed by fitting photon counting histograms and by filtering the image for pixels with intensities greater than a threshold value. The motivation of this analysis was to see if condensates can be identified from deviations in intensities. The results of the analysis indicated that deciphering noise in concentration from photon noise is challenging due to the temporal and spatial scale of transcriptional condensates existing at the limit of that of a confocal microscope.

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Session Classification: W3-3 Cell and Membrane Biophysics (DPMB) | Biophysique de la cellule et des membranes (DMPB)

Track Classification: Technical Sessions / Sessions techniques: Physics in Medicine and Biology / Physique en médecine et en biologie (DPMB-DPMB)