Contribution ID: **74** Type: **not specified**

Ribosome traffic jams underlie suppressive drug interactions

Wednesday 23 September 2020 14:40 (20 minutes)

The effects of antibiotics targeting protein synthesis are poorly understood when applied in combination. The combined antibiotic effect determines the type of drug interaction, which ranges from synergy to antagonism and suppression. In suppression, at least one of the drugs loses its potency in the presence of the second drug. We hypothesize that suppressive drug interactions result from the interplay between ribosomes halted in different stages of translation. We mimic this interplay by creating translation bottlenecks genetically by titration of translation factors. We rationalize the effects of translation bottlenecks by modeling dense traffic of ribosomes that move on transcripts in a translation factor-mediated manner. We base this model on the growth laws and quantitative relationships between different translation and growth parameters. This model predicts a dissolution of traffic jams caused by inhibited translocation when the density of ribosome traffic is reduced by lowered initiation, thus explaining suppression.

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Session Classification: Afternoon Session