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Stochastic modeling of sRNA-mRNA sequestration and reduction of translational burst noise in Vibrio quorum-sensing networks

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Interactions between biomolecules in DNA replication, transcription, and translation possess inherent stochasticity, which leads to intrinsic noise in gene expression (Elowitz et al., 2002). Organisms deploy various methods for regulating this noise to maintain precise RNA and protein levels. In Vibrio quorum-sensing networks, small, regulatory RNAs (sRNAs) called Qrr (Quorum regulatory RNA) regulate protein production by a sequestration mechanism in which luxO mRNA and a Qrr form a complex, sequestering the luxO mRNA ribosome-binding site and thus repressing translation (Feng et al., 2015). Previous mathematical models indicate that accelerated catalytic degradation of mRNAs by sRNAs can reduce protein noise in both prokaryotes (Levine et al., 2007, Mehta et al., 2008) and eukaryotes (Schmiedel et al., 2015). However, those models do not consider how the inhibition of translation by mRNA sequestration affects intrinsic noise in protein expression. Here, we extend existing models to address the sRNA-mRNA sequestration mechanism in bacterial regulatory networks. Like mRNA degradation, reversible sequestration of mRNA shortens the free-mRNA correlation time, reducing variation in resulting levels of translated protein, but without degrading the mRNA. By simulating this reaction network using the Gillespie stochastic simulation algorithm (SSA), we show that sequestration can dramatically reduce translational burst noise. At high sRNA levels, protein noise is reduced to the Poisson limit. We also demonstrate the existence of multiple distinct regimes of noise reduction depending on model parameters, revealing that protein noise reduction by mRNA sequestration is much more complex than previously thought. Our findings open avenues for further exploration into the feasibility of noise reduction by mRNA sequestration, with implications for microRNA-based noise regulation in eukaryotes.

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