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Gene dosage imbalance during DNA replication controls bacterial cell-fate decision[1]

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Genes encoding proteins in a common regulatory network are frequently located close to one another on the chromosome to facilitate co-regulation or couple gene expression to growth rate. Contrasting with these observations, here we demonstrate a functional role for the arrangement of *Bacillus subtilis* sporulation network genes on opposite sides of the chromosome. We show that the arrangement of two sporulation network genes, one located close to the origin, the other close to the terminus leads to a transient gene dosage imbalance during chromosome replication. This imbalance is detected by the sporulation network to produce cell-cycle coordinated pulses of the sporulation master regulator Spo0A~P. This pulsed response allows cells to decide between sporulation and continued vegetative growth during each cell-cycle spent in starvation. Furthermore, changes in DNA replication and cell-cycle parameters with decreased growth rate in starvation conditions enable cells to indirectly detect starvation without the need for evaluating specific metabolites. The simplicity of the uncovered coordination mechanism and starvation sensing suggests that it may be widely applicable in a variety of gene regulatory and stress-response settings.

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