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Collective synchronization of divisions in Drosophila development.[1]

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Mitoses in the early development of most metazoans are rapid and synchronized across the entire embryo. While diffusion is too slow, in vitro experiments have shown that waves of the cell-cycle regulator Cdk1 can transfer information rapidly across hundreds of microns. However, the signaling dynamics and the physical properties of chemical waves during embryonic development remain unclear. We develop FRET biosensors for the activity of Cdk1 and the checkpoint kinase Chk1 in Drosophila embryos and exploit them to measure waves in vivo. We demonstrate that Cdk1 chemical waves control mitotic waves and that their speed is regulated by the activity of Cdk1 during the S-phase (and not mitosis). We quantify the progressive slowdown of the waves with developmental cycles and identify its underlying control mechanism by the DNA replication checkpoint through the Chk1/Wee1 pathway. The global dynamics of the mitotic signaling network illustrates a novel control principle: the S-phase activity of Cdk1 regulates the speed of the mitotic wave, while the Cdk1 positive feedback ensures an invariantly rapid onset of mitosis. Mathematical modeling captures the speed of the waves and predicts a fundamental distinction between the S-phase Cdk1 trigger waves and the mitotic phase waves, which is illustrated by embryonic ablation experiments.

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