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**Sources of non-linearity in the mitotic trigger**

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Quantitative biochemical studies have shown that the Cdk1/APC system, which drives entry into and exit from mitosis, functions as a relaxation oscillator. The bistable switch for the oscillator is provided by the Cdk1/Wee1/Cdc25 sub-system, which consists of a pair of mirror-image positive feedback and double-negative feedback loops. In turn, the bistable switch relies on the ultrasensitive sigmoidal response functions of the two loops' components. Here we have investigated the mechanisms through which Wee1 and Cdc25 generate ultrasensitive responses. Our results argue that the ultrasensitivity arises mainly through cooperative multisite phosphorylation and competition.