

Workshop: *Deconstructing Biochemical Networks*  
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*Amplitude and Frequency Control in Two  
Classes of Biological Oscillator*

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**Abstract**

Under the proper circumstances a simple negative feedback loop of genes or proteins can function as a biological oscillator. However, two of the best characterized biological oscillators—the Hodgkin-Huxley oscillator in the sino-atrial node and the cell cycle oscillator—possess an additional circuit feature, a positive feedback loop that functions as a bistable trigger. This raises the question of what advantages the positive-plus-negative feedback design might have over a plain negative feedback design. Here we address this question by examining the performance of various oscillator models from the literature, as well as three oscillator models that are simple enough to allow parameter space to be sampled more comprehensively. We show that positive-plus-negative feedback oscillators, unlike negative feedback oscillators, can be adjusted over a wide range of periods or frequencies without substantially changing their amplitudes. The combination of an adjustable frequency and an invariant amplitude may be particularly advantageous for oscillators driving biological rhythms like heartbeats and cell cycles.