

CHARACTERIZATION OF
AMPLITUDE-TIMESCALE CO-VARIATIONS IN
BIOMOLECULAR SYSTEMS

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CHARACTERIZATION OF AMPLITUDE-TIMESCALE CO-VARIATIONS IN BIOMOLECULAR SYSTEMS

by

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Department of Electrical Engineering

Submitted

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Certificate

This is to certify that the thesis entitled “**Characterization of Amplitude-Timescale Co-variations in Biomolecular Systems**”, submitted by **Venkat Bokka** to the Indian Institute of Technology Delhi, for the award of the degree of **Doctor of Philosophy** in Electrical Engineering, is a record of the original, bona fide research work carried out by him under my supervision and guidance. The thesis has reached, to the best of my understanding, the standards fulfilling the requirements of the regulations related to the award of the degree.

The results contained in this thesis have not been submitted either in part or in full to any other university or institute for the award of any degree or diploma to the best of my knowledge.

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Abstract

Characterization of biomolecular systems is an important step for their analysis, design and control. Specifically, from a design perspective, possible co-variations of functionally important properties and robustness of the function to uncertainties are important to characterize. For cyclical systems such as cell cycles or oscillators, these are relatively less known. Using computations and experimental measurements, we address these issues in this thesis. We consider a phenomenological example of bacterial growth measurement and note the inverse co-variations between the maximum specific growth rate and growth duration as the temperature is varied. As a design constraint, trade-off between bacterial growth rate and its duration, may help to design biomolecular circuits that are robust to temperature. Using mathematical models of twelve benchmark biomolecular oscillators, we characterized the co-variations between maximum amplitude and period of oscillations and categorized the parameters into different types of co-variation trends. Next, we repeated the classification using a power norm-based amplitude metric, to account for the amplitudes of the many biomolecular species that may be part of the oscillations, finding largely similar trends. For a subset of oscillators, we find scaling laws of period-amplitude co-variation to find that as the approximated period increases the upper bound of amplitude increases or remains constant. Based on these results, we discuss the effect of different parameters on the type of period-amplitude co-variation as well as the difficulty in achieving an oscillation with large amplitude and short period. We find numerical evidence suggesting that an increase in sensitivity of period to a parameter can be compensated with a decrease in sensitivity to other parameter. We find evidence, using state sensitivity equation, for such trends in a cycle of oscillations as well. This characterization of amplitude-timescale co-variations should help with understanding the available design space of such cyclical systems.

सार

बायोमोलेक्युलर सिस्टम की विशेषता उनके विश्लेषण, डिजाइन और नियंत्रण के लिए एक महत्वपूर्ण कदम है। विशेष रूप से, एक डिजाइन के नजरिए से, कार्यात्मक रूप से महत्वपूर्ण गुणों के संभावित सह-रूपांतर और फंक्शन की अनश्चितताओं की अनश्चितता को चिह्नित करना महत्वपूर्ण है। सेल साइकल या ऑसिलेटर जैसी चक्रीय प्रणालियों के लिए, ये अपेक्षाकृत कम ज्ञात हैं। कम्प्यूटेशन और प्रायोगिक मापों का उपयोग करते हुए, हम इन मुद्दों को इस थीसिस में संबोधित करते हैं। हम जीवाणु विकास माप का एक अभूतपूर्व उदाहरण मानते हैं और अधिकतम विशिष्ट विकास दर और वृद्धि की अवधि के बीच व्युत्क्रम सह-विविधताओं पर ध्यान देते हैं क्योंकि तापमान भिन्न होता है। एक डिजाइन बाधा के रूप में, बैक्टीरियल विकास दर और इसकी अवधि के बीच व्यापार बंद, तापमान को मजबूत करने वाले बायोमोलेक्युलर सर्किट को डिजाइन करने में मदद कर सकता है। बारह बैचमार्क बायोमोलेक्युलर ऑसिलेटर्स के गणितीय मॉडल का उपयोग करते हुए, हमने अधिकतम आयाम और दोलनों की अवधि के बीच सह-विविधताओं की विशेषता की और मापदंडों को विभिन्न प्रकार के सह-रूपांतर प्रवृत्तियों में वर्गीकृत किया। इसके बाद, हमने कई जैव-आणविक प्रजातियों के आयामों का लेखा-जोखा करने के लिए एक शक्तिमानक-आधारित आयाम मीटर के उपयोग करके वर्गीकरण को दोहराया, जो मोटे तौर पर समान रुझानों को खोजने के लिए दोलनों का हिसा हो सकता है। ऑसिलेटर्स के एक सबसेट के लिए, हम अवधि-आयाम सह-भिन्नता के स्केलिंग कानूनों को खोजने के लिए पाते हैं कि जैसा कि अनुमानित अवधि बढ़ जाती है आयाम के ऊपरी सीमा बढ़ जाती है या स्थिर रहती है। इन परिणामों के आधार पर, हम विभिन्न आयामों के प्रभाव पर अवधि-आयाम सह-भिन्नता के प्रकार के साथ-साथ बड़े आयाम और छोटी अवधि के साथ दोलन प्राप्त करने में कठिनाई पर चर्चा करते हैं। हम संख्यात्मक प्रमाणों का सुझाव देते हुए कहते हैं कि एक पैरामीटर के लिए अवधि की संवेदनशीलता में वृद्धि से दूसरे पैरामीटर के लिए संवेदनशीलता में कमी के साथ क्षतिपूर्ति की जा सकती है। हम साक्ष्य पाते हैं, राज्य संवेदनशीलता समीकरण का उपयोग करते हुए, दोलन के एक चक्र में ऐसी प्रवृत्तियों के लिए भी। आयाम-टाइमसेल सह-विविधताओं का यह लक्षण वर्णन ऐसे चक्रीय प्रणालियों के उपलब्ध डिजाइन स्थान को समझने में मदद करना चाहिए।

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