

# Decoding High-dimensional Temporal Dynamics in Gene-regulatory Networks

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**Recent advances in visualization of single molecules, such as transcription factors with temporal resolution in single cells, have shown that information is transmitted through time-varying dynamics of components shared between multiple pathways. This phenomenon stands in contrast to the typical paradigm where information is transmitted via structurally specific interactions (e.g. the lock and key model). Consequently, signaling through time dynamics via shared components raises natural questions about how such interactions can effect only the intended response. By analyzing realistic, coarse-grained regulatory networks informed by experimental studies, we find the design principles for regulatory circuits that respond to specific characteristics of an input time-series, such as frequency, duty cycle or pulse number, while buffering variations in other aspects. Our results show which aspects of time-varying input patterns need to varied independently in experiments to fully understand the signaling capacity of a multiplexed regulatory pathway.**

## I. PURPOSE

CELLS are constantly exposed to a dynamically changing environment; often survival hinges on the capability to extract meaningful information from this environment and respond appropriately. The capability of biochemical circuits to respond to temporal patterns in a specific manner has been explicitly established experimentally in a wide range of systems, ranging from bacterial to mammalian cells [1]. Here, we aim to understand the origins of these networks’ capability of faithful temporal decoding mechanistically. By analyzing experimental data and numerically simulating coarse-grained gene-regulatory network models, we describe what aspects of temporal data are accessible to these networks. Further, we identify key mechanisms for recognizing specific features in a time-series and construct explicit models capable of such processing.

## II. RESULTS

### A. Dimensionality in the Yeast *Msn2* System

We introduce our own model-independent quantification of network decoding fidelity which we have termed *specificity*. By calculating this quantity for a set of genes coupled to *Msn2* dynamics [2] and operating under the reasonable assumption of monotonicity of response to larger doses of the input, we are able to definitively state that this

system is able to access more than a single dimension of the temporal input.

### B. Mechanisms for Temporal Decoding

In contrast, any linear time-invariant (LTI) system must have its integrated output proportional to the area of the input time-series (in accordance with the Convolution Theorem). Motivated by this divergence between LTI systems and the observed processing in the *Msn2* system, we chose four features (amplitude, period, duty fraction, and pulse number) to characterize a space of time-varying inputs and built nonlinear models able to respond to each feature independently.

### C. Temporal Decoding and Circuit Topology

In establishing our mechanisms for temporal decoding, the importance of circuit topology was evident. For example, adaptation was found to be central to sensing period and pulse number, and it is known that only specific network topologies are capable of such dynamics [3]. To generalize our findings, we numerically optimized sets of networks using our *specificity* as an objective function for the task of decoding a fixed set of input pulse-trains with restrictions on the type of connections allowed (thus restricting accessible topologies over the course of the optimization procedure). The optimum obtained is strongly dependent on both the allowed topologies of the search and the distinguishing features of the input pulse trains, exhibiting the critical relationship between encoding method and decoder design.

## III.

## CONCLUSIONS

By introducing specificity, a model-independent quantification of decoding efficacy, we are able to observe multidimensional temporal decoding in data from the *Msn2* system. Informed by this, we explicitly construct models capable of decoding in a four-dimensional space of pulsatile inputs. Our results suggest when

## REFERENCES

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