

## Signal-Response Modeling of Partial Hormone Feedback Networks

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### Abstract

#### **Background:**

Endocrine feedback control networks are typically complex and contain multiple hormones, pools, and compartments. The hormones themselves commonly interact via multiple pathways and targets within the networks, and a complete description of such relationships may involve hundreds of parameters. In addition, it is often difficult, if not impossible, to collect experimental data pertaining to every component within the network. Therefore, the complete simultaneous analysis of such networks is challenging. Nevertheless, an understanding of these networks is critical for furthering our knowledge of hormonal regulation in both physiologic and pathophysiologic conditions.

#### **Methods:**

We propose a novel approach for the analysis of dose-response relationships of subsets of hormonal feedback networks. The algorithm and signal-response quantification (SRQuant) software is based on convolution integrals, and tests whether several discretely measured input signals can be individually delayed, spread in time, transformed, combined, and discretely convolved with an elimination function to predict the time course of the concentration of an output hormone. Signal-response quantification is applied to examples from the endocrine literature to demonstrate its applicability to the analysis of the different endocrine networks.

#### **Results:**

In one example, SRQuant determines the dose-response relationship by which one hormone regulates another, highlighting its advantages over other traditional methods. In a second example, for the first time (to the best of our knowledge), we show that the secretion of glucagon may be jointly controlled by the  $\beta$  and the  $\delta$  cells.

#### **Conclusion:**

We have developed a novel convolution integral-based approach, algorithm, and software (SRQuant) for the analysis of dose-response relationships within subsets of complex endocrine feedback control networks.

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**Abbreviations:** (AIC) Akaike information criterion, (CV) coefficient of variation, (FWHH) full-width at half-height, (GH) growth hormone, (GnRH) gonadotropin-releasing hormone, (LH) luteinizing hormone, (SRIF) somatostatin/somatotropin release-inhibiting factor, (SRQuant) signal-response quantification, (XApEn) cross approximate entropy

**Keywords:** data analysis, data modeling, hormonal networks, hormone oscillations, pulsatility

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