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Title: From empirical protocols to feedback-controlled therapy: closed-loop opportunities in IVF stimulation

ABSTRACT

This study presents a minimal four-state ordinary differential equation (ODE) model that reproduces the core dynamics of the menstrual cycle while incorporating hypothalamic–pituitary–adrenal (HPA) stress coupling. The model was derived through systematic reduction of four previously published high-fidelity models, retaining only the essential feedback mechanisms required for self-sustained oscillatory behaviour. The reduced system describes estradiol, luteinising hormone, corpus luteum activity, and progesterone, while follicle-stimulating hormone is represented implicitly through progesterone-mediated inhibition. Regulatory interactions are captured using Hill functions to model nonlinear activation and inhibition thresholds, including the steep estradiol-driven LH surge.

Despite containing only four state variables and seventeen parameters, the model reproduces the sequential follicular, ovulatory, and luteal phases with physiologically realistic hormone concentrations and timescales. The framework provides a compact yet biologically grounded representation of menstrual endocrine dynamics, enabling efficient simulation of cycle regulation and perturbations such as stress-induced suppression of reproductive hormones.