

**Invitation to M.Tech. Thesis Defense of Harika G L: August 04, 2023 (Friday): 12:00 Noon – 01:00 PM IST**

In Partial Fulfillment of the Requirements for the Degree of

**M.Tech. CB**

**Harika G L (MT20339)**

Will defend her thesis

**Title: “Structural, Kinetic, and dynamical analysis of receptor-activated proteolysis”**

IIIT-D Faculty and Students are invited

**Date: August 04, 2023 (Friday)
Time:** **12:00 Noon – 01:00 PM IST**

**Venue Details:** **A-320, 3rd Floor, R&D Bui**

**lding**

**Examiner: Internal:   G. P. S .Raghava**

**External/~~Internal~~: Ganesh Bagler**

**Advisor: K. Sriram**

**Co-Advisor NA**

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**Abstract**

One of the challenging tasks in systems-level modelling is determining the bistable dynamics from the networks constructed from the experiments. A necessary but not sufficient condition for bistability is the presence of positive feedback motifs in the network. In many cases, one can easily identify positive feedback by visual inspection if the network is constructed properly from the experiments. But there are cases where positive feedback is implicit, and it is not straightforward to determine its presence in the network. A quick way to determine bistability from the biological network is to perform structural analysis using chemical reaction network theory (CRNT). CRNT is a powerful tool that can not only determine bistability but also provide kinetic parameters that one can use profitably to construct bifurcation diagrams to verify the presence of bistability numerically. However, the drawback in CRNT is that the kinetic parameters are not close to what is obtained from the experiments. Therefore, kinetic parameters must be separately determined from the experimental data. They can be obtained directly from the experiments or extracted by fitting the steady state or time series data. However, the estimated kinetic parameters need not give rise to bistability, and in that case, either the parameters have to be recalibrated, or one has to discard the old mechanism and propose a new one. We demonstrate the usefulness of this structural and kinetic analysis to a recently proposed signal transduction pathway for receptor-mediated proteolysis (RMP), where this pathway is triggered during amino-acid starvation. We proposed many mechanisms for RMP network dynamics where the feedback loops are hidden in the network. Structural analysis indicated that all the mechanisms exhibited bistability. A subnetwork also exhibited transcritical bifurcation. However, to perform kinetic analysis, sufficient data were not available and with the available data, the parameters were recalibrated to exhibit bistability. Overall, all the mechanisms seem plausible, and the resolution about the right mechanism, structure, and dynamics can only be arrived at if we get more data from the experiments.