STRATEGIES FOR E-CADHERIN RECYCLING: A COMPUTATIONAL MODEL

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BTP-1 MID-TERM PRESENTATION

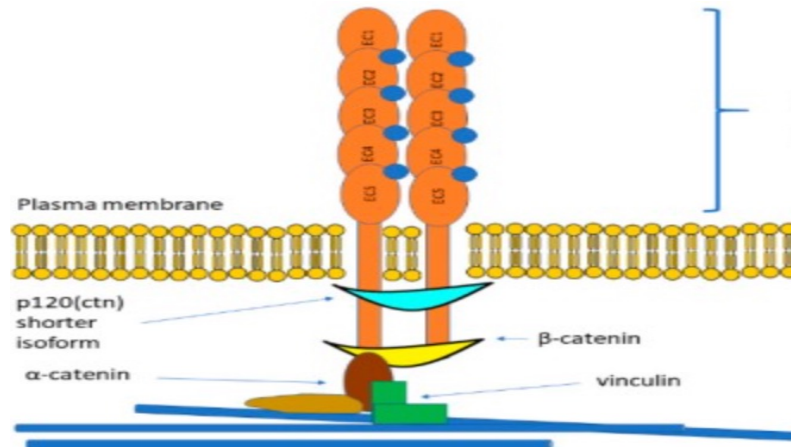GUIDED BY: PROFESSOR AMIT DAS

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INTRODUCTION

Figure 1.1 A number of cytoplasmic proteins, including beta-catenin, alpha- catenin, and p120 catenin, engage with the intracellular domain of E-cadherin
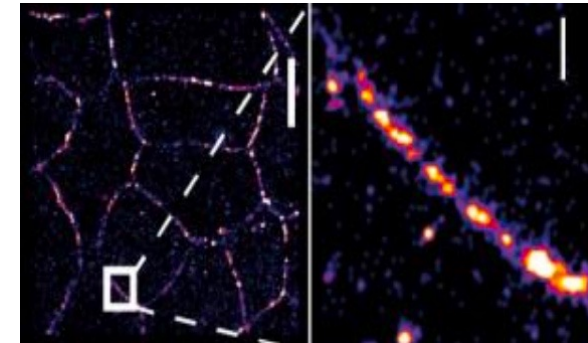

Figure 1.2 Supramolecular organization of E-cad. Higher magnification (bottom) shows uneven dense regions along a cell junction.

Communication Among Cells via Adhesion Molecules

Role of E-cadherin

E-cadherin and Proteins

MOTIVATION

GOAL: To incorporate E-cadherin Recycling mechanism and explore its impact on the E-cadherin clustering via a Computational Model

Recycling and its three ways

Why is understanding E-cadherin recycling important?
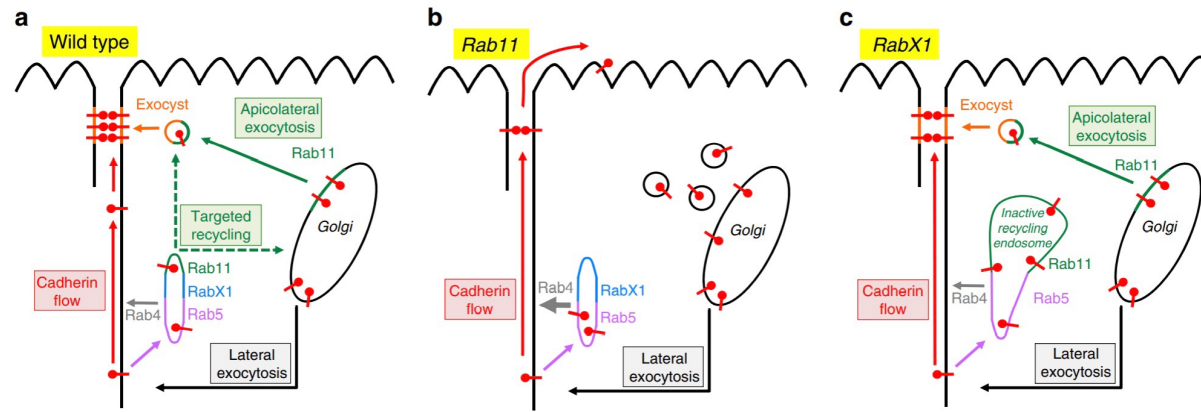
Cluster Formation and Endocytosis

Figure 2.1 Model depicting the three ways via which E-cadherin recycling takes place, Wild Type, Rab11 and RabX1

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METHOD

The Langevin Equation: A Tool we used for Regulating Protein Molecule Motion

$$\frac{d^2 x}{dt^2} = -\Gamma \frac{dx}{dt} + F_{int} + F_{random} \quad \text{----------------------} (1)$$

Here, Γ is the friction coefficient, dX/dt indicates the velocity of the particle, F int denotes the force of interaction between particles, and F random represents the force arising from the unpredictable motion of the surrounding fluid or environment.

$$\Gamma \frac{dx}{dt} = F_{random} = v_0 \, \hat{n} \quad \text{-------------------------} (2)$$

Here, v_0 is the is the characteristic velocity of the protein molecules arising from F-actin, And $\hat{n}$ is a unit vector that points in a random direction at any instant.
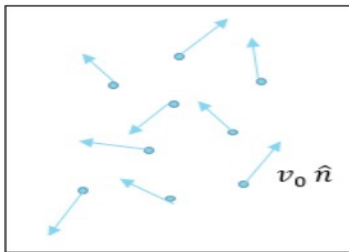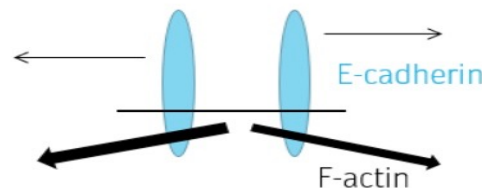

Fig 3.1 Random movement of E-cadherin molecules

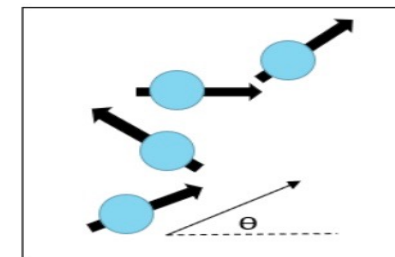Fig 3.2 Active movement of E-cadherin molecule by F-actin

Fig 3.3 Top-view of the cell membrane showing active movement of E-cad

METHOD

To tackle the recycling mechanism we considered all the three
Recycling methods for E-cadherin to be in a Black Box. This helped us
Get the molecules in and out of the mechanism to be added back onto the
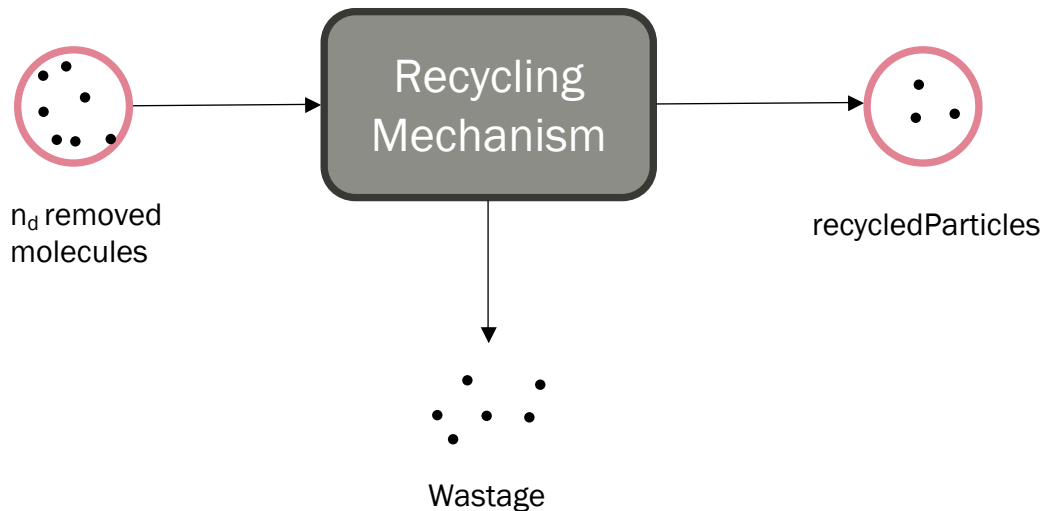Cell surface in a relatively easier manner.

n_d removed molecules at t=100
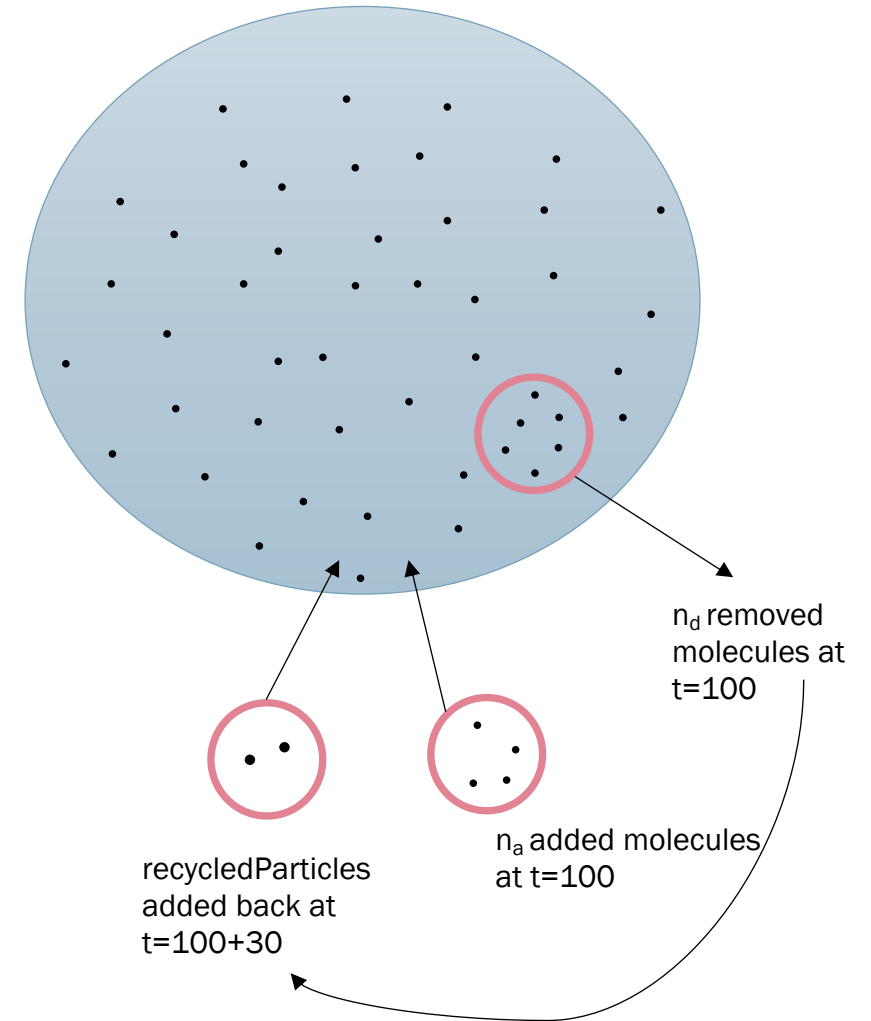
recycledParticles added back at t=100+30

n_a added molecules at t=100

Fig 3.5 Graphic showing E-cadherin Recycling, Exocytosis and Endocytosis in a Nutshell

Recycling Mechanism

n_d removed molecules

recycledParticles

Wastage

Fig 3.4 Recycling Mechanism for E-cad in a cell simplified

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RESULTS AND DISCUSSION

Current Model

Previous Model
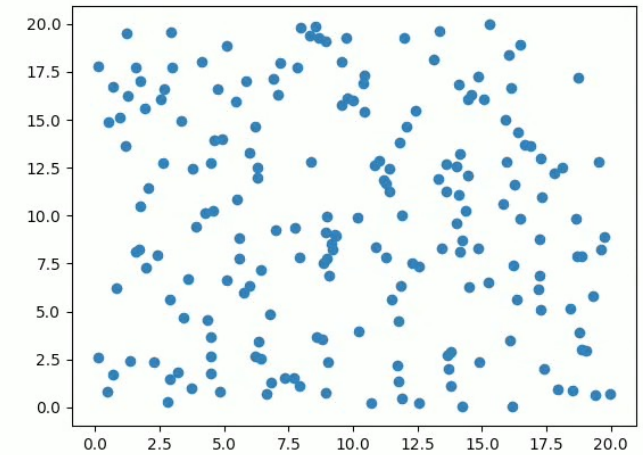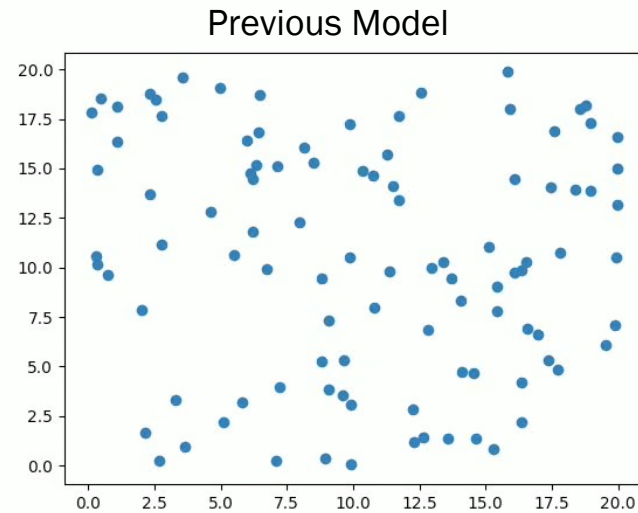
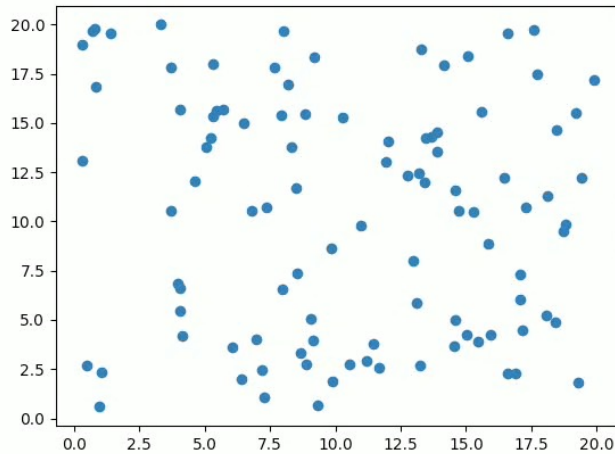

Fig 4.1 Cell Surface when Endocytosis rate is equal to Exocytosis rate from t=0 to t=10000 starting with 100 molecules
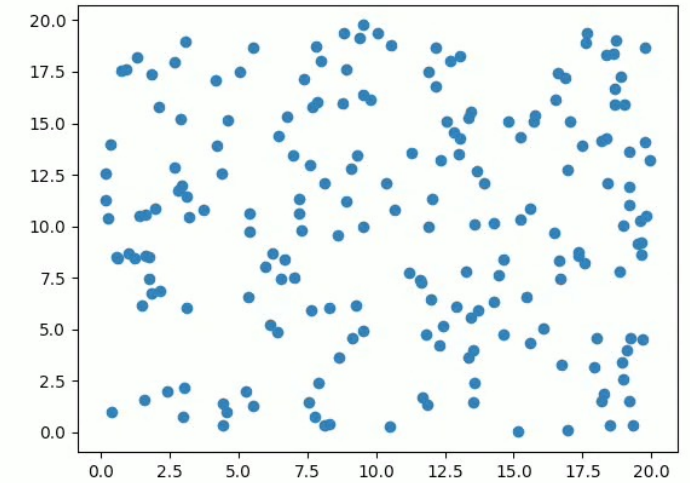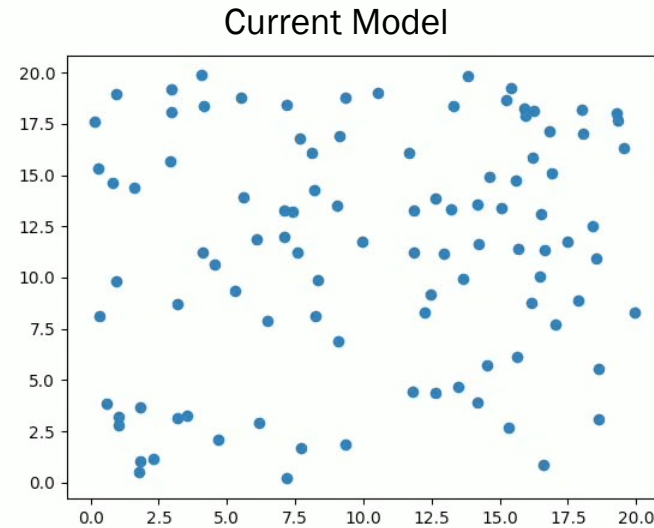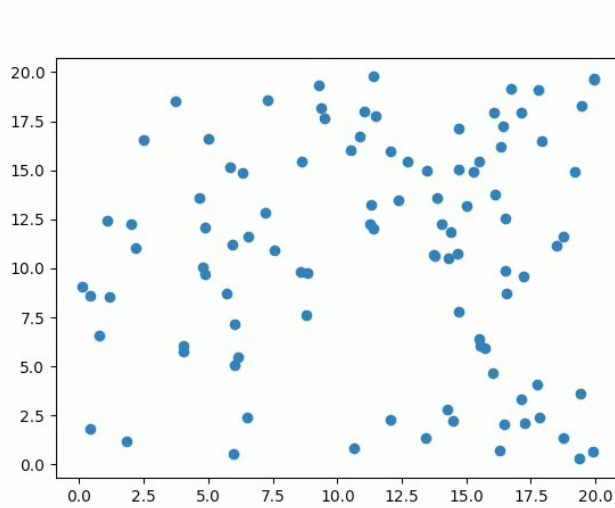
Fig 4.2 Cell Surface when Endocytosis rate is lesser than Exocytosis rate from t=0 to t=10000 starting with 100 molecules

Fig 4.3 Cell Surface when Endocytosis rate is greater than Exocytosis rate from t=0 to t=10000 starting with 200 molecules

FUTURE PLAN

Breaking down the recycling processes → Interplay between the recycling processes → Dynamic Model that interacts with itself

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THANK YOU!

Any Questions?