

# Cell Collective:

Enabling accessible and collaborative construction and analysis of comprehensive and annotated models

Tomas Helikar

[www.cellcollective.org](http://www.cellcollective.org) || [www.helikarlab.org](http://www.helikarlab.org) || @helikarlab || thelikar2@unl.edu

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# Our goal:



1. ELIMINATE THE BAR

And Make Modeling **Accessible** to ANYONE



Cell Collective: <https://cellcollective.org>

The screenshot shows the Cell Collective website homepage. At the top left is the logo 'Cell Collective'. Below it is a navigation bar with three tabs: 'Student' (grey), 'Teacher' (grey), and 'Researcher' (orange). A large green banner features a microscopic image of a cell. Below the banner, a main heading reads: 'Build large-scale models of biological systems, validate, simulate, perturb, and analyze data'. Three main sections are listed: 'Build Models' (with a molecular icon), 'Simulate' (with a graph icon), and 'Distribute' (with a network icon). Each section has a brief description. At the bottom is a large orange button labeled 'Get Started as Researcher'.

Cell Collective

Student Teacher Researcher

Build large-scale models of biological systems, validate, simulate, perturb, and analyze data

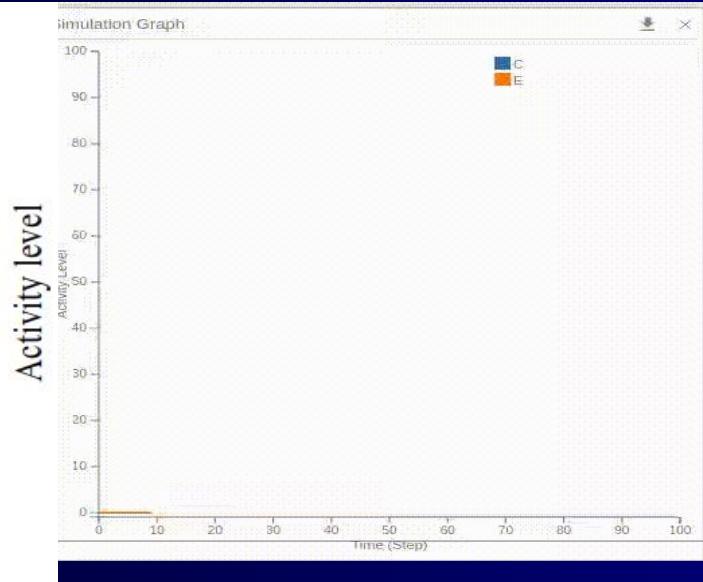
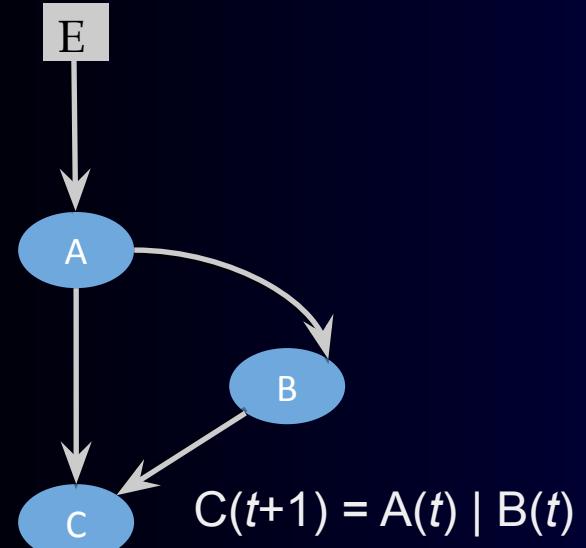
Build Models  
Collaboratively construct and annotate comprehensive mechanistic models

Simulate  
Interactively simulate and analyze biological behaviors using a variety of built-in tools

Distribute  
Share, distribute, and re-use models for and within the scientific community

Get Started as Researcher

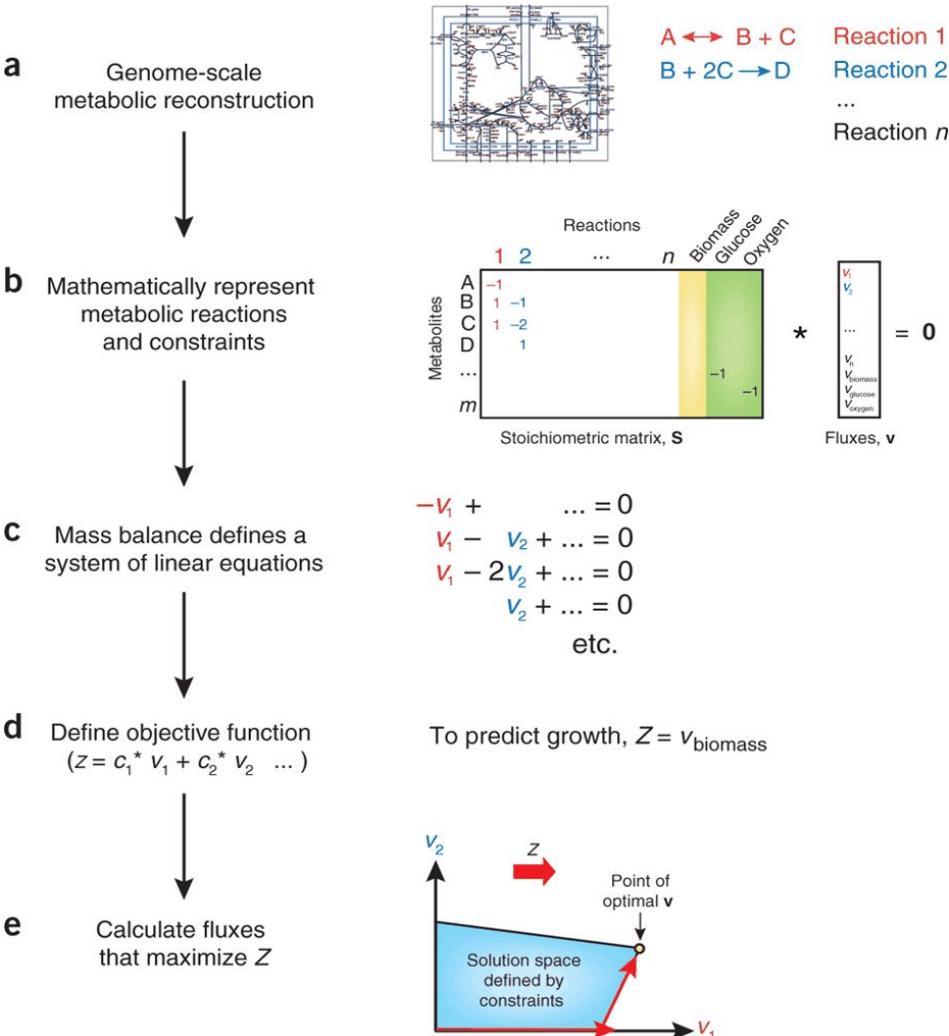
# Logical Models in Cell Collective



- Qualitative logic, i.e., “Proteins A or B activates protein C”
- (Kinetic) parameter independent
- Efficient simulations
- Delays (i.e., update after X steps of receiving an activation signal)
- Thresholds (i.e., update after X number of activating signals)
- Knowledge Base for detailed annotation

# Constraint-based Models

- Flux Balance Analysis
- Flux Variability Analysis
- Custom Objective Function
- Context-specific Model Creation
- Define Gene Regulation
- Multi-layer Network Navigation
- Knowledge Base for detailed annotation





# Model Building

cellcollective  
RESEARCH

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Bacterial Chemotaxis  
version 1.0

Graph Layout New Layout 1

Model Simulation Analysis Network Analysis Knowledge Base Description

Internal Components

Name		

Regulatory Mechanism

Positive Regulators	Negative Regulators

External Components

Name

Knowledge Base

Component	Description



# Multi-layer model visualization and navigation

Multi-scale model navigation

## ccNetViz: a WebGL-based JavaScript library for visualization of large networks

Ales Saska, David Tichy, Robert Moore, Achilles Rasquinha, Caner Akdas, Xiaodong Zhao, Renato Fabbri, Ana Jelićić, Gaurav Grover, Himanshu Jotwani, Mohamed Shadab, Resa M Helikar, Tomáš Helikar

*Bioinformatics*, Volume 36, Issue 16, 15 August 2020, Pages 4527–4529,

<https://doi.org/10.1093/bioinformatics/btaa559>

Published: 09 June 2020 Article history ▾



# Model Simulations & Analysis: Real-Time Simulations

chemotaxis test  
version 1.0

Model Simulation Analysis Network Analysis Knowledge Base Description

Simulation Control

Activity Network

Layout: New Layout 1

Repellent Attractant

Rep\_Rec Att\_Rec

CheB CheW

CheA CheY

Motor Run Tumble

Simulation Graph

Time (Step)



# Model Simulations & Analysis: Dose-response / Titrations

Experiment Settings

Completed: 100%

Name: New Experiment 1

Number of Simulations: 1000

Environment New Env 2

Initial State All Inactive

Output Range (500-800)

Updating: Synchronous

Generate Bits

Simulation Flow None

Experiments

Name	Created	Run
New Experiment 1	9/7/2019	<input checked="" type="checkbox"/>
New Experiment 2	10/7/2019	<input type="checkbox"/>

External Components

Env: New Env 2

Activity Range

Name	Activity Range
Attractant	0 % <input type="radio"/> 100 % <input type="radio"/>
Repellent	0 % <input type="radio"/> 9 % <input type="radio"/>

Activity Relationships Graph

The graph plots Activity Level (Y-axis, 0-100) against Attractant (Activity Level) (X-axis, 0-100). Blue dots represent the 'Run' component, which increases from ~50 at 0% attractant to ~95 at 100% attractant. Orange dots represent the 'Tumble' component, which decreases from ~50 at 0% attractant to ~5 at 100% attractant.

Legend: Run (Blue), Tumble (Orange)

Y-axis: Activity Level

X-axis: Attractant (Activity Level)

Graph Components

Search

Name	X	Y
Att_Rec	<input type="checkbox"/>	<input type="checkbox"/>
Attractant	<input checked="" type="checkbox"/>	<input type="checkbox"/>
CheA	<input type="checkbox"/>	<input type="checkbox"/>
CheB	<input type="checkbox"/>	<input type="checkbox"/>
CheW	<input type="checkbox"/>	<input type="checkbox"/>
CheY	<input type="checkbox"/>	<input type="checkbox"/>
Motor	<input type="checkbox"/>	<input type="checkbox"/>
Rep_Rec	<input type="checkbox"/>	<input type="checkbox"/>
Repellent	<input type="checkbox"/>	<input type="checkbox"/>
Run	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Tumble	<input type="checkbox"/>	<input checked="" type="checkbox"/>

Internal Components

Search

Name	Run	Tumble
Att_Rec	<input type="checkbox"/>	<input type="checkbox"/>
CheA	<input type="checkbox"/>	<input type="checkbox"/>
CheB	<input type="checkbox"/>	<input type="checkbox"/>
CheW	<input type="checkbox"/>	<input type="checkbox"/>
CheY	<input type="checkbox"/>	<input type="checkbox"/>
Motor	<input type="checkbox"/>	<input type="checkbox"/>
Rep_Rec	<input type="checkbox"/>	<input type="checkbox"/>
Run	<input type="checkbox"/>	<input type="checkbox"/>
Tumble	<input type="checkbox"/>	<input type="checkbox"/>



# Model Simulations & Analysis: Environment Sensitivity Analysis

bacterial chemotaxis  
version 1.0

Model Simulation Analysis Network Analysis Knowledge Base Description

Experiments

Name	Created	Run Status
When do I run the most?	9/6/2019	100%

External Components

Name	Activity Range
Attractant	0 % — 100 %
repellent	0 % — 100 %

Component sensitivity for Run

Correlation

Attractant repellent

Experiment Settings

Completed: 100% Elapsed: 0s

Name: When do I run the most?

Number of Simulations: 1000

Environment Default

Initial State All Inactive

Output Range (500-800)

Updating: Synchronous

Generate Bits

Internal Components

Name	States
CheB	Off, On
ChevW	Off, On
ChevY	Off, On
Motor	Off, On
Rep_Rec	Off, On
Run	Off, On
Tumble	Off, On

Environment Sensitivity

Attractant repellent



# Model Simulations & Analysis: Feedback loop analysis



bacterial chemotaxis  
version 1.0



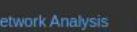
Model



Simulation



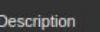
Analysis



Network Analysis



Knowledge Base



Description

Tomas Helikar

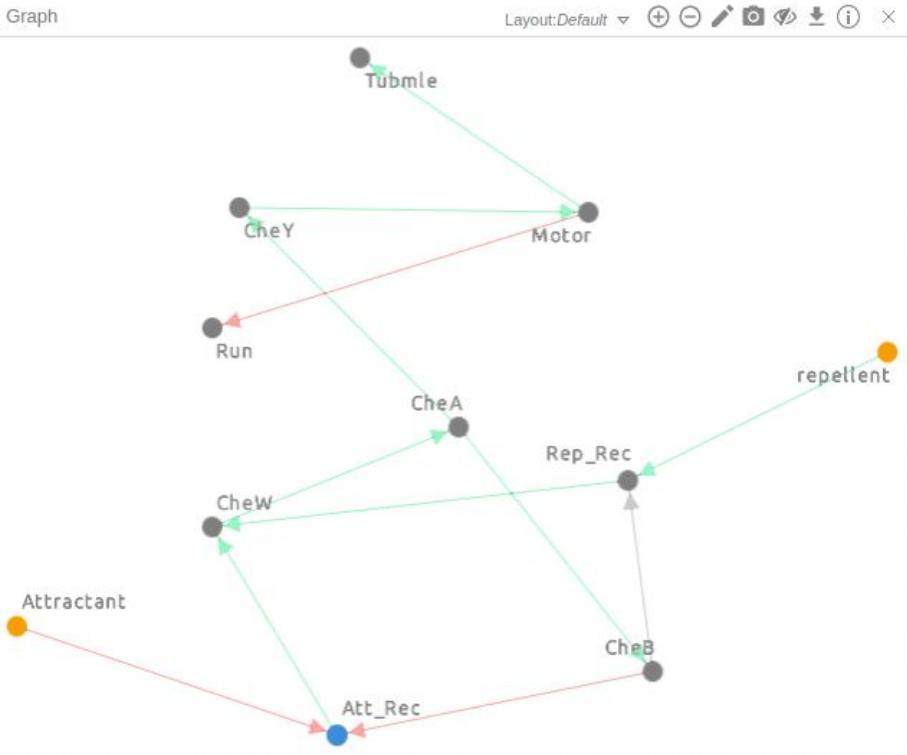


Feedback Loops List

Feedback Loops

id	Feedback Loops
0	Rep_Rec -> CheW -> CheA -> CheB -> Rep_Rec
1	CheW -> CheA -> CheB -> Att_Rec -> CheW
2	CheW -> CheA -> CheB -> Rep_Rec -> CheW
3	Att_Rec -> CheW -> CheA -> CheB -> Att_Rec

Graph





# Model Simulations & Analysis: State Space Analysis

cellcollective  
research

Bacterial Chemotaxis  
version 1.0



Model

Simulation

Analysis

Network Analysis

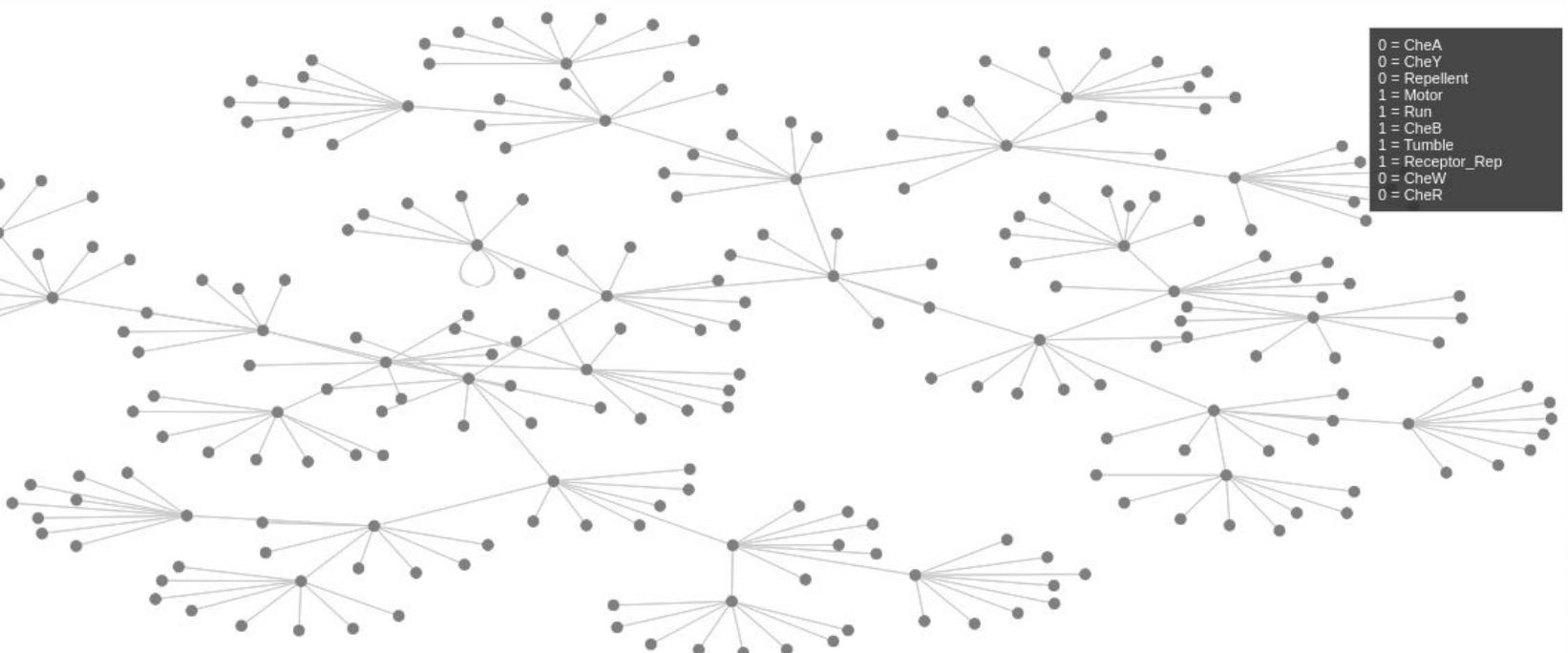
Knowledge Base

Description

Tomas Helikar



State Transition Graph



# Our goal:



1. ELIMINATE THE BAR

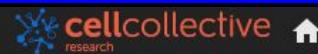
And Make Modeling **Accessible** to ANYONE

2. UNVEIL THE MECHANISM

Annotate and Explain



# Cell Collective: Models annotation and transparency



Tomas Helikar



IGVH mutations in chronic lymphocytic leukemia.

Knowledge Base Simulation Analysis Model Description
□ Download 2

Components
<span>Search</span>
Name
ADM
AEBP1
AFF1
AICDA
AKAP12
AKT3
ALOX5
ANXA2
APLP2
APOBEC3G
APP
BLNK
BMI1
CASP3
CAV1
CCL5
CCND2
CD27
CD63
CD69
CD70

## Knowledge Base ADM

### Description +

- Adrenomedullin
- Gene ID: 133
- ADM and PAMP act as hypotensive and vasodilator agents. Both mediate the loss of plasma volume in the brain and pituitary gland and inhibit aldosterone secretion. (Álvarez-Silva MC, 2015)
- Gene: ADM
- UniProt ID: P35318

### Regulatory Mechanism Summary +

HSP90AA1 or TNF in conjunction with HSP0AA1 activates ADM. (Hofbauer KH, 2002)  
(Masoud GN, 2015)

### Upstream Regulators

#### HSP90AA1

HSP90AA1 indirectly upregulates ADM expression. (Masoud GN, 2015)

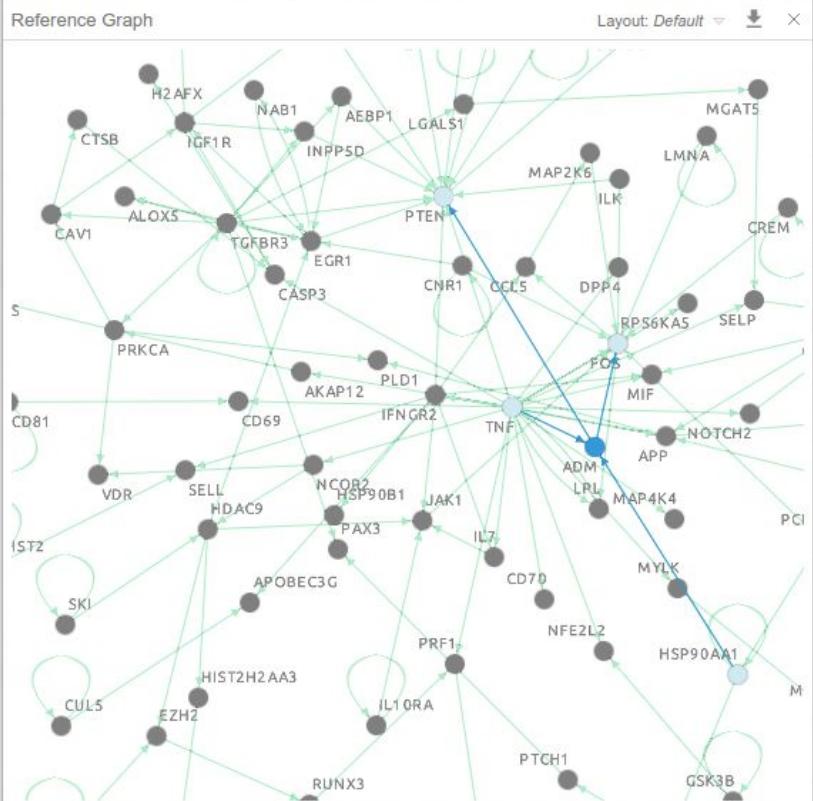
#### TNF

Cells treated with TNF showed upregulation of ADM mRNA. (Hofbauer KH, 2002)

### References ≡

- Hofbauer KH, Schoof E, Kurtz A, and Sandner P. Inflammatory cytokines stimulate adrenomedullin expression through nitric oxide-dependent and -independent pathways. *Hypertension* 2002 Jan;39;(1) 161-7. pmid:11799096
- Masoud GN and Li W. HIF-1 $\alpha$  pathway: role, regulation and intervention for cancer therapy. *Acta Pharm Sin B* 2015 Sep;5;(5) 378-89. pmid:26579469
- Álvarez-Silva MC, Yépez S, Torres MM, and Barrios AF. Protein interaction network and modeling

## Reference Graph





# Cell Collective: Models annotation and transparency



Tomas Helikar



IGVH mutations in chronic lymphocytic leukemia. Knowledge Base Simulation Analysis Model Description

**Components**

- Name**
- ADM
- AEBP1
- AFF1
- AICDA
- AKAP12
- AKT3
- ALOX5
- ANXA2
- APLP2
- APOBEC3G
- APP
- BLNK
- BMI1
- CASP3
- CAV1
- CCL5
- CCND2
- CD27
- CD63
- CD69
- CD70

**Knowledge Base ADM**

**Description**

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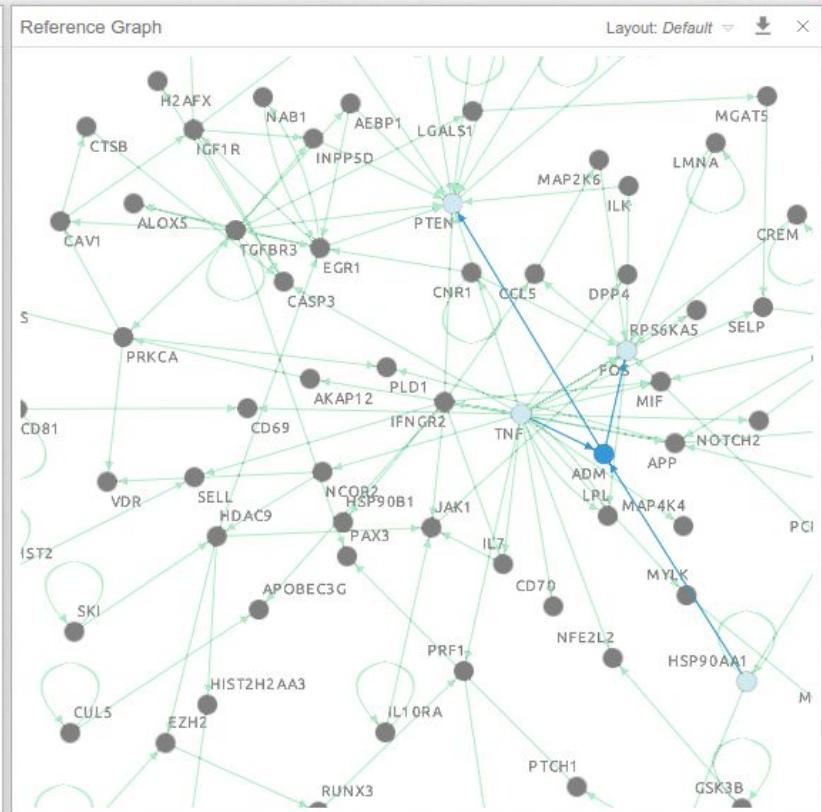
**Upstream Regulators**

**HSP90AA1**  
HSP90AA1 indirectly upregulates ADM expression. (Masoud GN, 2015)

**TNF**  
Cells treated with TNF showed upregulation of ADM mRNA. (Hofbauer KH, 2002)

**References**

1. Hofbauer KH, Schoof E, Kurtz A, and Sandner P. Inflammatory cytokines stimulate adrenomedullin expression through nitric oxide-dependent and -independent pathways. *Hypertension* 2002 Jan;39(1) 161-7. pmid:11799096
2. Masoud GN and Li W. HIF-1 $\alpha$  pathway: role, regulation and intervention for cancer therapy. *Acta Pharm Sin B* 2015 Sep;5(5) 378-89. pmid:26579469
3. Álvarez-Silva MC, Yépez S, Torres MM, and Bardos AF. Proteins interaction network and modeling.



# Our goal:



## 1. ELIMINATE THE BAR

And Make Modeling **Accessible** to ANYONE

## 2. UNVEIL THE MECHANISM

Annotate and Explain

## 3. COLLABORATE

To **Construct** More Detailed, Comprehensive  
and Accurate Models

To Use Models to **Discover**



# Collaboration, Repository, and Model Access



SBML Qual Paper Final Model demo



Knowledge Base

## Simulation

## Analysis

## Model

### Description

#### Share with Collaborators



 Search

Email



tr

Model cannot be published.

## Publishing requirements

- ✗ *Model has to have been included in at least one peer-reviewed publication.*  
There are no publications associated with this model (You can add publications under the Description page).
  - ✗ *Each model component should be annotated in the knowledge base in an effort to make models more reproducible, transparent and accessible to the community.*

Components without knowledge base information:

A grid of 16 protein names representing a network of interactions. The rows are labeled 'akt', 'ap1', 'ask1', 'cjun', 'creb', 'egf', 'egfr', 'erk', 'ex', 'gsk3', 'ikb', 'ikk', 'jnk', 'map3k1', 'map3k7', and 'mek'. The columns are labeled 'mkk4', 'mkk7', 'nflkb', 'nik', 'p38', 'p90rsk', 'nb', 'ni3k', 'rsf1', 'ras', 'sos', 'tnfa', 'tnfr', and 'traf2'. Edges connect nodes between adjacent positions in both rows and columns, indicating interactions.

*User profile of the model owner has to be filled.*

## Shareable Links



Search

## Link



1

<https://cellcollective.org/#a2b73520-ffc4>

 TM

rheumatoid arthritis map  
version 1

Graph Layout:rheumatoid arthritis map Model Simulation Analysis Network Analysis Knowledge Base Description

Internal Components

Name	Value	Condition
ABL1	2	
ACT1	1	
Actin Based Motility, Cell Migration	1	
active_cAMP	1	
actived_H_sub_2_endsub_O_sub_2	1	
ADAMTS-9	1	
ADCY7	1	
ADM	3	
AKT2	2	
Apoptosis	9	

External Components

Name
ABL1
ACT1
ADAMTS-9

Regulatory Mechanism ABL1

Positive Regulators: Drop Component

Negative Regulators: Drop Component

ABL1

Conditions +

Condition

If/When EPHA4 is Active

SubConditions +

SubCondition

If/When CRKL is Inactive

Knowledge Base ABL1

CRKL

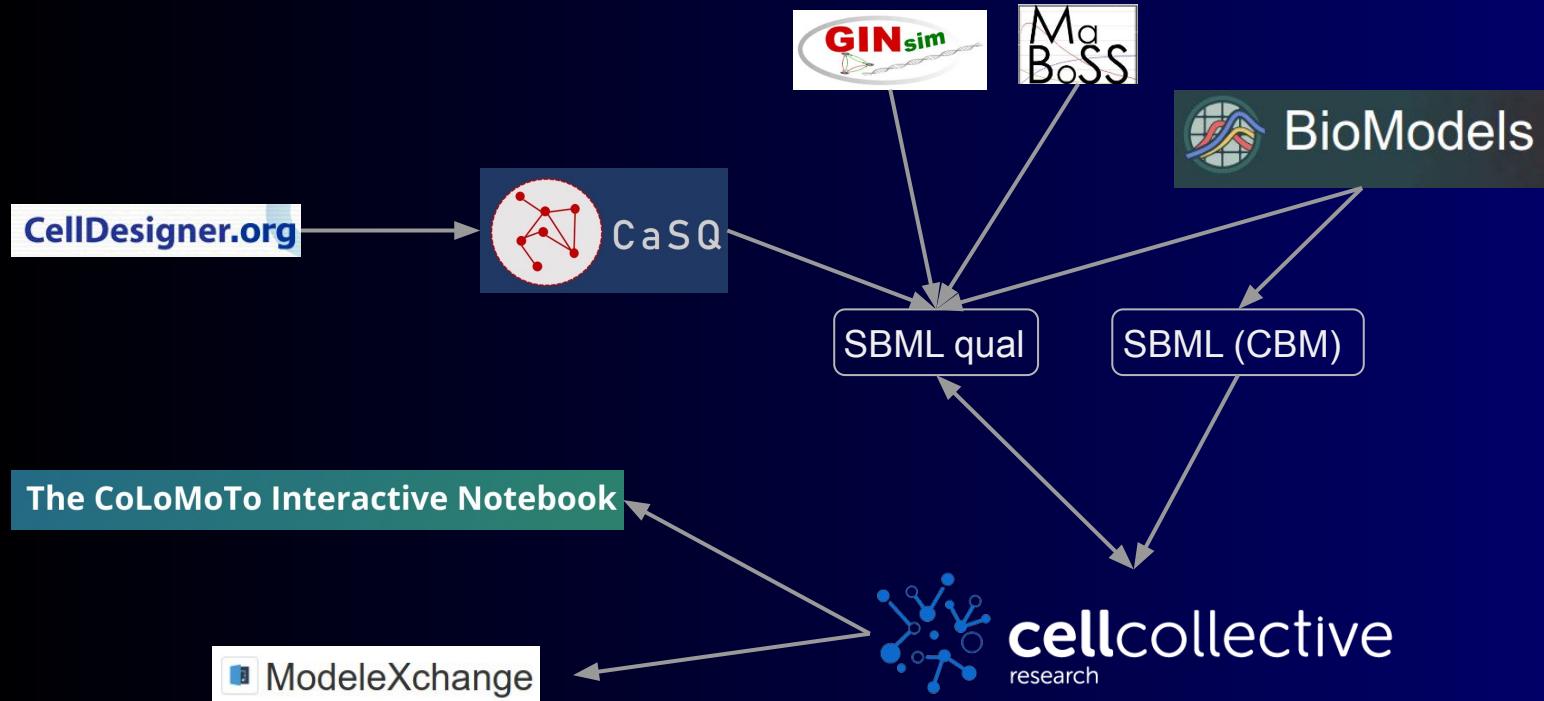
EPHA4

References

- Lindberg J, af Klint E, Catrina AI, Nilsson P, Klareskog L, Ulfgren AK, and Lundeberg J. Effect of infliximab on mRNA expression profiles in synovial tissue of rheumatoid arthritis patients. *Arthritis Res Ther* 2006; (6) R179. pmid:17134501



# Cell Collective - Ecosystem & Collaboration





# Cell Collective: Collaboration and Model Repository

Published Models (226) My Models (55) Shared With Me (319)

No Filter

## RECENTLY PUBLISHED

*Trypanosoma cruzi Dm28c*

Approach: Constraint-Based

Metabolites: 606 Reactions: 520



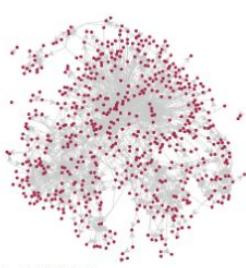
Author: Cell Collective

Score: Cited: 0  
Created: 1/29/2021 Updated: 1/29/2021

*Trypanosoma cruzi Dm28c*

Approach: Constraint-Based

Metabolites: 606 Reactions: 519



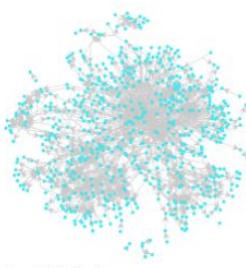
Author: Cell Collective

Score: Cited: 0  
Created: 1/29/2021 Updated: 1/29/2021

*Trypanosoma cruzi Dm28c*

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Metabolites: 606 Reactions: 519



Author: Cell Collective

Score: Cited: 0  
Created: 1/29/2021 Updated: 1/29/2021

*Trypanosoma cruzi Dm28c*

Approach: Constraint-Based

Metabolites: 606 Reactions: 519



Author: Cell Collective

Score: Cited: 0  
Created: 1/29/2021 Updated: 1/29/2021

## MOST POPULAR

*Guard Cell Abscisic Acid Signaling*

Approach: Logical

Components: 44 Interactions: 78



Author: S Li et. al.

Score: Cited: 307  
Created: 6/20/2013 Updated: 7/19/2017

*HGF Signaling in Keratinocytes*

Approach: Logical

Components: 68 Interactions: 103



Author: A Singh et. al.

Score: Cited: 17  
Created: 9/13/2012 Updated: 7/12/2017

*IL-1 Signaling*

Approach: Logical

Components: 118 Interactions: 218



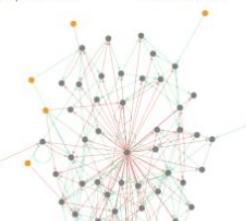
Author: Ryll A et. al.

Score: Cited: 17  
Created: 8/26/2013 Updated: 5/18/2017

*T-LGL Survival Network 2008*

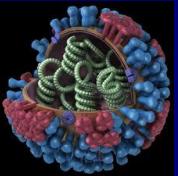
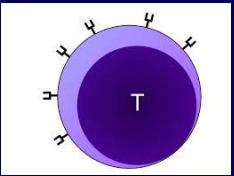
Approach: Logical

Components: 61 Interactions: 193



Author: R Zhang et. al.

Score: Cited: 176  
Created: 6/26/2013 Updated: 5/15/2017



# Our goal:



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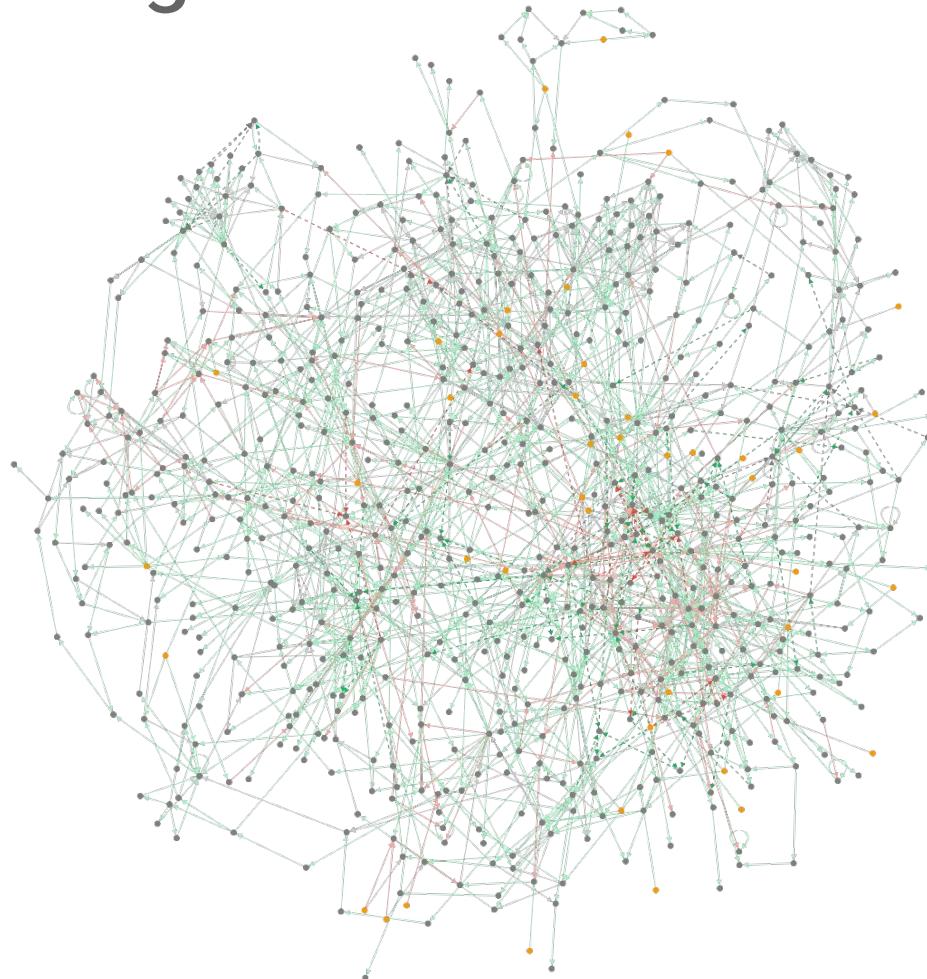
## 2. UNVEIL THE MECHANISM

Annotate and Explain

## 4. DON'T REINVENT THE WHEEL

And Allow Others **Re-Use** and **Reproduce**  
your Work

# But, how do I get started with this .... mess ...?



# Custom Interactive Model Guides

Simulating the Behavior of Cellular Respiration (163274)

File Insert Edit Workspace Reports Help

Overview Start Here

Page 1 Page 2 Page 3 Page 4 Page 5

Cellular Respiration Cellular Respiration No Glucose Pyruvate Processing Inhibited Pyruvate Processing Inhibited

1. Simulation of the cellular respiration system behavior

The purpose of this simulation is to explore how the inputs and outputs of each process of cellular respiration impact the activity of the entire system. We'll walk you through how to set the simulation controls, and then ask you to describe the model behavior once you play the simulation.

- Within the Activity Network panel, click the following components to change them grey-blue; this two-toned component color means they will be visible within the Simulation Graph, once the simulation is played.
  - glycolysis
  - pyruvate\_processing
  - citric\_acid\_cycle
  - electron\_transport\_chain
- Within the External Components panel, set all External components to 100%. This means that all external stimuli are available and active.
- Set the Sliding Window to "100".
- Start the simulation by clicking on the *play* button in the Simulation Control panel; pause after ~80 time steps.

Activity Network

Layout: Cellular Respiration

External Components

Environment: Default

Simulation Control

Simulation Graph

Detailed description: The screenshot shows a simulation guide for 'Cellular Respiration' (ID 163274). The top navigation bar includes 'File', 'Insert', 'Edit', 'Workspace', 'Reports', and 'Help'. Below the tabs are five panels: 'Overview' (selected), 'Start Here', 'Page 1: Cellular Respiration', 'Page 2: Cellular Respiration', and 'Page 3: No Glucose'. The main content area has three sections: 'Activity Network' (a directed graph of metabolic pathways like glycolysis, pyruvate\_processing, citric\_acid\_cycle, and electron\_transport\_chain), 'External Components' (a table of substances with activity levels at 0%), and 'Simulation Control' (with sliders for Speed, Sliding Window, Initial State, and Updating mode). The 'Simulation Graph' at the bottom shows fluctuating activity levels over 100 time steps.

# Custom Interactive Model Guides

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Cellular Respiration Cellular Respiration No Glucose Pyruvate Processing Inhibited Pyruvate Processing Inhibited

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Activity Network

Layout: Cellular Respiration

External Components

Environment: Default

Simulation Control

Simulation Graph

# Custom Interactive Model Guides

Simulating the Behavior of Cellular Respiration (163274)

File Insert Edit Workspace Reports Help

Overview Start Here

Page 1 Page 2 Page 3 Page 4 Page 5

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Activity Network

Layout: Cellular Respiration

External Components

Environment: Default

Simulation Control

Simulation Graph

1. glucose  
2.NAD+  
3.ADP  
4.ATP  
5.FAD+  
6.oxygen  
fatty\_acid\_metabolism  
1.glycolysis  
2.pyruvate\_processing  
3.citric\_acid\_cycle  
4.electron\_transport\_chain  
5.CO2\_production  
6.H2O\_production  
7.lactate\_production  
8.NADH\_FADH2\_pool  
9.NADH\_FADH2\_pool\_PP  
10.ATP\_pool\_CAC  
11.ATP\_pool\_ETC  
12.ATP\_pool\_glycolysis  
13.pyruvate\_pool  
14.acetyl\_CoA\_pool

Name	Activity
1.glucose	0 %
2.NAD+	0 %
3.ADP	0 %
4.ATP	0 %
5.FAD+	0 %
6.oxygen	0 %
fatty_acid_metabolism	0 %

Time (Step)

# Custom Interactive Model Guides

Exploring Prokaryotic Gene Regulation in the Lac Operon (118235) - changes not saved

File Insert Edit Workspace Help

Resa Helikar

Overview 1. Build the Glucose Path 2. Build the Lactose Path 3. Predict Model Behavior 4. Simulate Behavior 5: Mutation Simulations 6. Strengths/Limitations

Step 1: Build Glucose Path Step 2: Build Glucose Path Step 3: Build Glucose Path Step 4: Build Glucose Path Step 5: Build Glucose Path Step 6: Build Glucose Path

1.0 1.0 1.0 1.0 1.0 1.0

Model Building Questions 1

Graph Layout: New Layout 4

Feel free to navigate back to previous sections of the lesson to find the best answers. Save before switching steps so you will not lose any answers. You are also encouraged to use the connections in your model as a resource to help you answer the following questions when possible.

Q1. The only signal detected by the lac operon is environmental lactose.

Participation Model Building No Objective Points: 1

Options:  True  False

Q2. The lac operon detects both glucose and lactose signals from the environment.

Participation Model Building No Objective Points: 1

Options:  True  False

Participation Model Building

Discuss the lac operon as a prokaryotic gene regulation system and its overall importance for controlling lactose digestion

Points: 1

Q3. The lac operon is an inducible gene regulation system that controls the production of enzymes that digest lactose.

Participation Model Building

Options:  True  False

The diagram shows two orange circular nodes labeled "Glucose" and "Lactose". They are positioned at opposite ends of a horizontal line segment, which is connected to a small orange dot in the center. This visual representation likely indicates that the lac operon can detect both glucose and lactose signals.

# Custom Interactive Model Guides

Exploring Prokaryotic Gene Regulation in the Lac Operon (118235) - changes not saved

File Insert Edit Workspace Help

Resa Helikar

Overview 1. Build the Glucose Path 2. Build the Lactose Path 3. Predict Model Behavior 4. Simulate Behavior 5: Mutation Simulations 6. Strengths/Limitations

Step 1: Build Glucose Path Step 2: Build Glucose Path Step 3: Predict Model Behavior Step 4: Simulate Behavior Step 5: Build Glucose Path Step 6: Build Glucose Path

Model Building Questions 1

Graph Layout: New Layout 4

Feel free to navigate back to previous sections of the lesson to find the best answers. Save before switching steps so you will not lose any answers. You are also encouraged to use the connections in your model as a resource to help you answer the following questions when possible.

Q1. The only signal detected by the lac operon is environmental lactose.

Participation Model Building No Objective Points: 1

Options: +

True  False

Q2. The lac operon detects both glucose and lactose signals from the environment.

Participation Model Building No Objective Points: 1

Options: +

True  False

Participation Model Building

Discuss the lac operon as a prokaryotic gene regulation system and its overall importance for controlling lactose digestion

Q3. The lac operon is an inducible gene regulation system that controls the production of enzymes that digest lactose.

Participation Model Building

Options: +

True  False



Glucose

Lactose

# Custom Interactive Model Guides

Exploring Prokaryotic Gene Regulation in the Lac Operon (118235) - changes not saved

File Insert Edit Workspace Help

Overview 1. Build the Glucose Path 2. Build the Lactose Path 3. Predict Model Behavior 4. Simulate Behavior 5: Mutation Simulations 6. Strengths/Limitations

Step 1: Build Glucose Path 1.0 Step 2: Build Glucose Path 1.0 Step 3: Build Glucose Path 1.0 Step 4: Build Glucose Path 1.0 Step 5: Build Glucose Path 1.0 Step 6: Build Glucose Path 1.0

Model Building Questions 1

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Feel free to navigate back to previous sections of the lesson to find the best answers. Save before switching steps so you will not lose any answers. You are also encouraged to use the connections in your model as a resource to help you answer the following questions when possible.

Q1. The only signal detected by the lac operon is environmental lactose.

Participation ▾ Model Building ▾ No Objective ▾ T  Points: 1

Options: +

True  False

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Participation ▾ Model Building ▾ No Objective ▾ T  Points: 1

Options: +

True  False

Participation ▾ Model Building ▾

Discuss the lac operon as a prokaryotic gene regulation system and its overall importance for controlling lactose digestion

Q3. The lac operon is an inducible gene regulation system that controls the production of enzymes that digest lactose.

Participation ▾ Model Building ▾

Options: +

True  False



# Custom Interactive Model Guides

Overview Start Here Page 1 1.0 Page 2 1.0 Page 3 1.0 Page 4 1.0 Page 5 1.0 Page 6 1.0 Submit Lesson 1.0

## 1. Model of light and dark reactions

On the right, a model of light and dark reactions in the process of photosynthesis has been built for you. Click on white space within the graph panel to de-select any components/arrows (in case you already started exploring!).

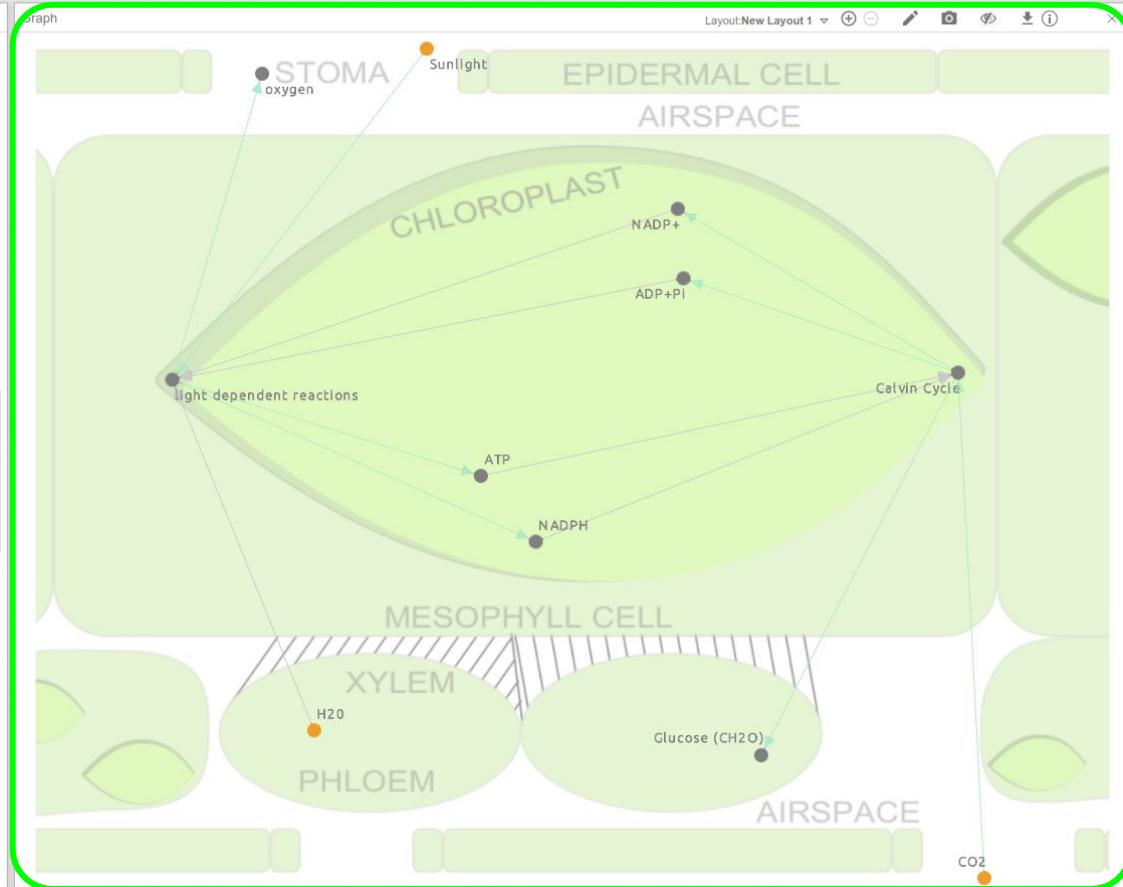
What you should notice in this model is the following:

- There are two processes occurring: light-dependent reactions and the Calvin Cycle.
- Matter is cycling between these two processes: ADP and NADPH are used during the Calvin Cycle where ATP is reduced to  $\text{ADP}+\text{Pi}$ , and NADPH is oxidized to  $\text{NADP}^+$ .  $\text{NADP}^+$  and  $\text{ADP}+\text{Pi}$  are then recharged during light-dependent reactions, back to ATP and NADPH.
- In order for light-dependent reactions to function, not only are  $\text{NADP}^+$  and  $\text{ADP}+\text{Pi}$  necessary, but  $\text{H}_2\text{O}$  and sunlight are also required.
- In order for the Calvin cycle to function, not only are ATP and NADPH required, but  $\text{CO}_2$  is also required.

Q1. Describe the energy    Assessment ▾ General Skills ▾ No Objective ▾ T  Points: 1

molecules that are generated by the light-dependent reactions and the energy molecules that are generated by the Calvin Cycle.

Example answer: The light-dependent reactions produce oxygen, ATP (for energy storage), and NADPH (the reduced electron carrier). The Calvin cycle uses both ATP and NADPH to produce  $\text{NADP}^+$ , ADP, and glucose. Both  $\text{NADP}^+$  and ADP are recycled and used in the light-dependent reactions.



# Our goal:



## 1. ELIMINATE THE BAR

And Make Modeling **Accessible** to ANYONE

## 3. COLLABORATE

To **Construct** More Detailed, Comprehensive  
and Accurate Models

To Use Models to **Discover**

## 2. UNVEIL THE MECHANISM

Annotate and Explain

## 4. DON'T REINVENT THE WHEEL

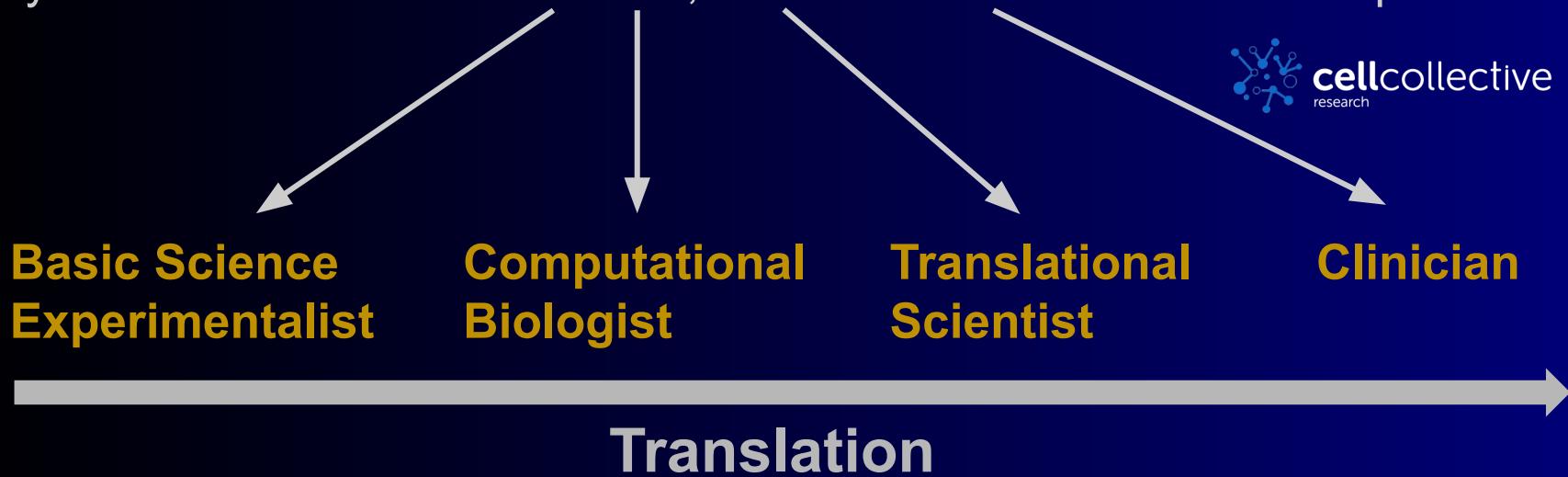
And Allow Others **Re-Use** and **Reproduce**  
your Work



## Cell Collective Long-term Vision

Accessible, scalable, integrative (multi-scale), and personalized computational platform....

..... to better understand and predict complex behavior of biological systems in the context of health, diseases and associated therapies.





Cell Collective: <https://cellcollective.org>

The screenshot shows the Cell Collective website homepage. At the top left is the logo "Cell Collective". Below it is a navigation bar with three tabs: "Student" (gray), "Teacher" (gray), and "Researcher" (orange). A large green banner features a microscopic image of a cell. Below the banner, a main heading reads: "Build large-scale models of biological systems, validate, simulate, perturb, and analyze data". Three main sections are listed: "Build Models" (with a molecular icon), "Simulate" (with a graph icon), and "Distribute" (with a network icon). Each section has a brief description. At the bottom is a large orange button labeled "Get Started as Researcher".

Cell Collective

Student Teacher Researcher

Build large-scale models of biological systems, validate, simulate, perturb, and analyze data

Build Models  
Collaboratively construct and annotate comprehensive mechanistic models

Simulate  
Interactively simulate and analyze biological behaviors using a variety of built-in tools

Distribute  
Share, distribute, and re-use models for and within the scientific community

Get Started as Researcher

# Our goal:

1. ELIMINATE THE BAR

And Make Modeling Attainable to  
ANYONE

2. Give students the  
**opportunity**

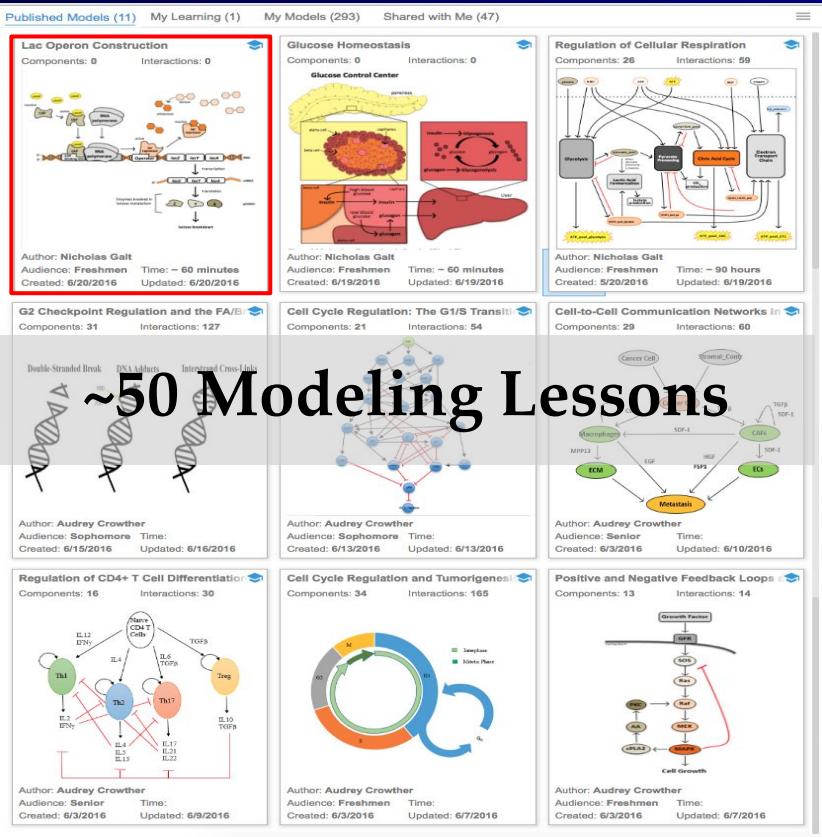
to practice, practice, and practice in  
**a constructivist, inquiry-based,**  
**and scientifically authentic**  
fashion



# Broad application of Cell Collective Modeling Lessons

## Key Lesson Design Features

- Model-building and simulations
- Self-contained
- Simple, turn-key implementation
- Predict/observe/explain scenarios
- Modular implementation
  - Laboratory activity
  - Homework
  - In-class activity





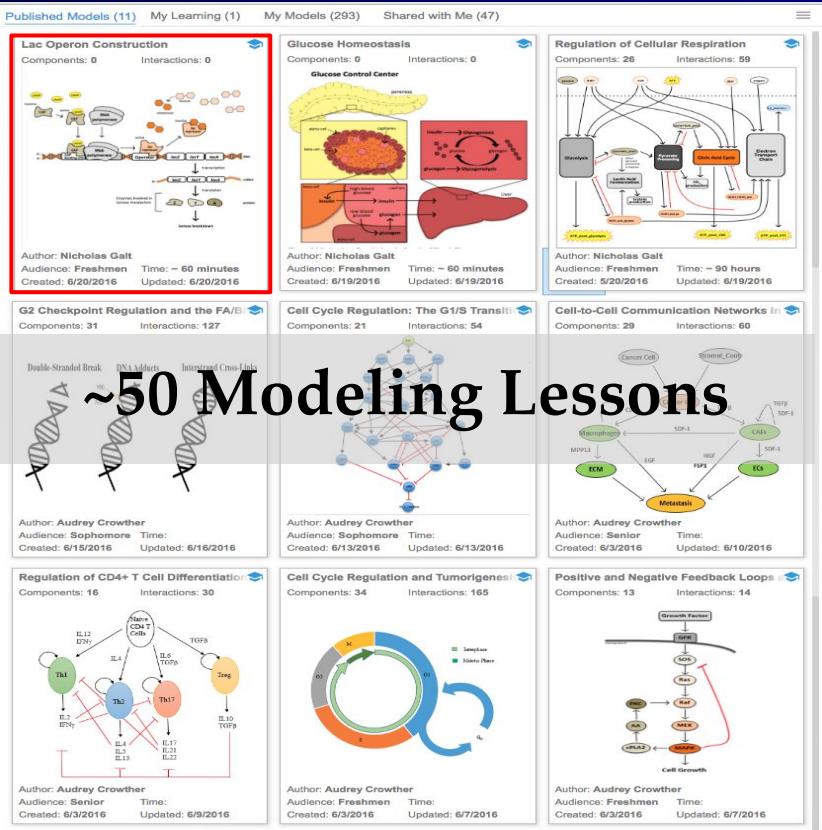
# Broad application of Modeling Lessons

## Topics

- Metabolism: Glycolysis, TCA cycle, ETC
- Cell respiration
- Glucose homeostasis
- Cell cycle
- Photosynthesis
- Gene regulation
- Food web dynamics

## Courses (high school - graduate)

- Biochemistry
- Intro biology courses
- Immunology
- Cancer Biology
- *Many others*



# Modeling lesson design

Build a model

Make prediction (*hypothesis generation*)

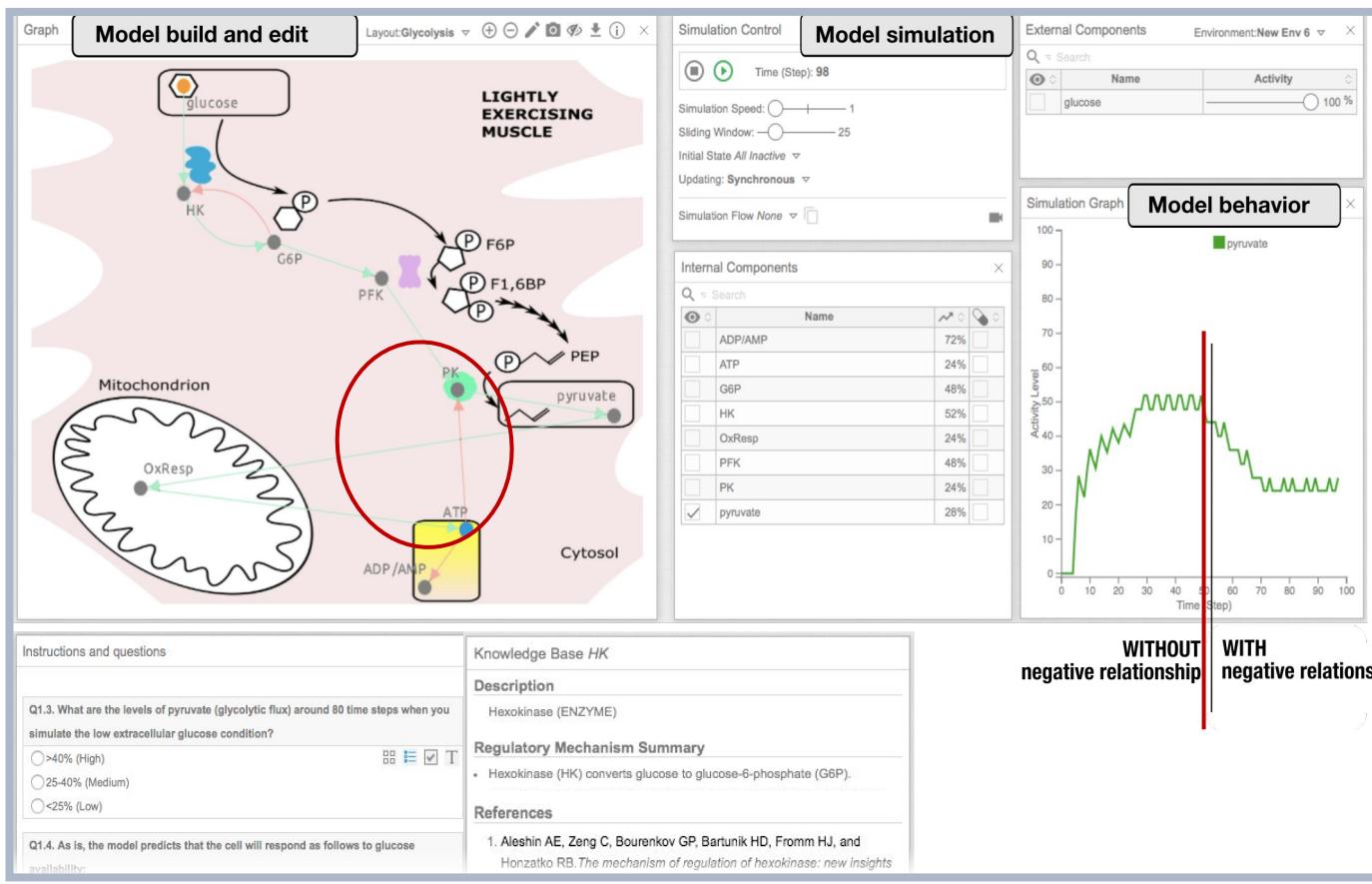
Justify prediction (*mechanistic thinking*)

Test prediction (*experimental design*)

Report simulation results (*data interpretation*)

Evaluate your prediction (*data interpretation*)

Refine prediction using simulation results (*mechanistic thinking, hypothesis generation*)





# Cell Collective World-wide Adoption

Published Models (77) My Models (42) Shared With Me (281)

RECENTLY PUBLISHED

HIV-1 Interactions with T Cell Signalling Pathway Version 1.0 Components: 138 Interactions: 138 Author: C. Created: Score: 45

T Cell Receptor Signaling Version 1.0 Components: 101 Interactions: 158 Author: A Fauré et. al. Created: 5/13/2014 Score: 132.8 Cited: 346 Updated: 7/19/2017

Signaling Pathway for Butanol Production in Clostridium beijerinckii NRRL B-598 Version 1.0 Components: 16 Interactions: 22 Author: S Li et. al. Created: 6/19/2013 Score: 106.2 Cited: 307 Updated: 7/19/2017

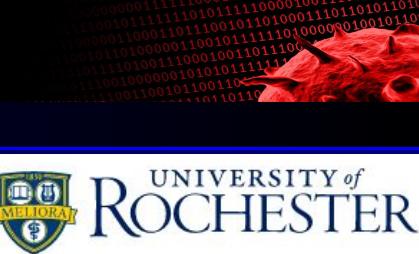
Neurotransmitter Signaling Pathway Version 1.0 Components: 16 Interactions: 22 Author: S Klamt et. al. Created: 2/9/2015 Score: 98.9 Cited: 306 Updated: 1/22/2016

Author: J Saez-Rodriguez et. al. Created: 6/23/2013 Score: 92.9 Cited: 220 Updated: 8/9/2019

It's a few seconds

MOST PUBLISHED

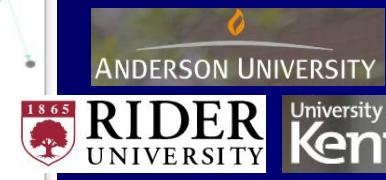
Mammal Version 1 Components: 138 Interactions: 138 Author: C. Created: Score: 45



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UNIVERSITY

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