Temperature and glucose concentration are two of many important factors when modeling *Saccharomyces cerevisiae* growth in a two nutrient chemostat

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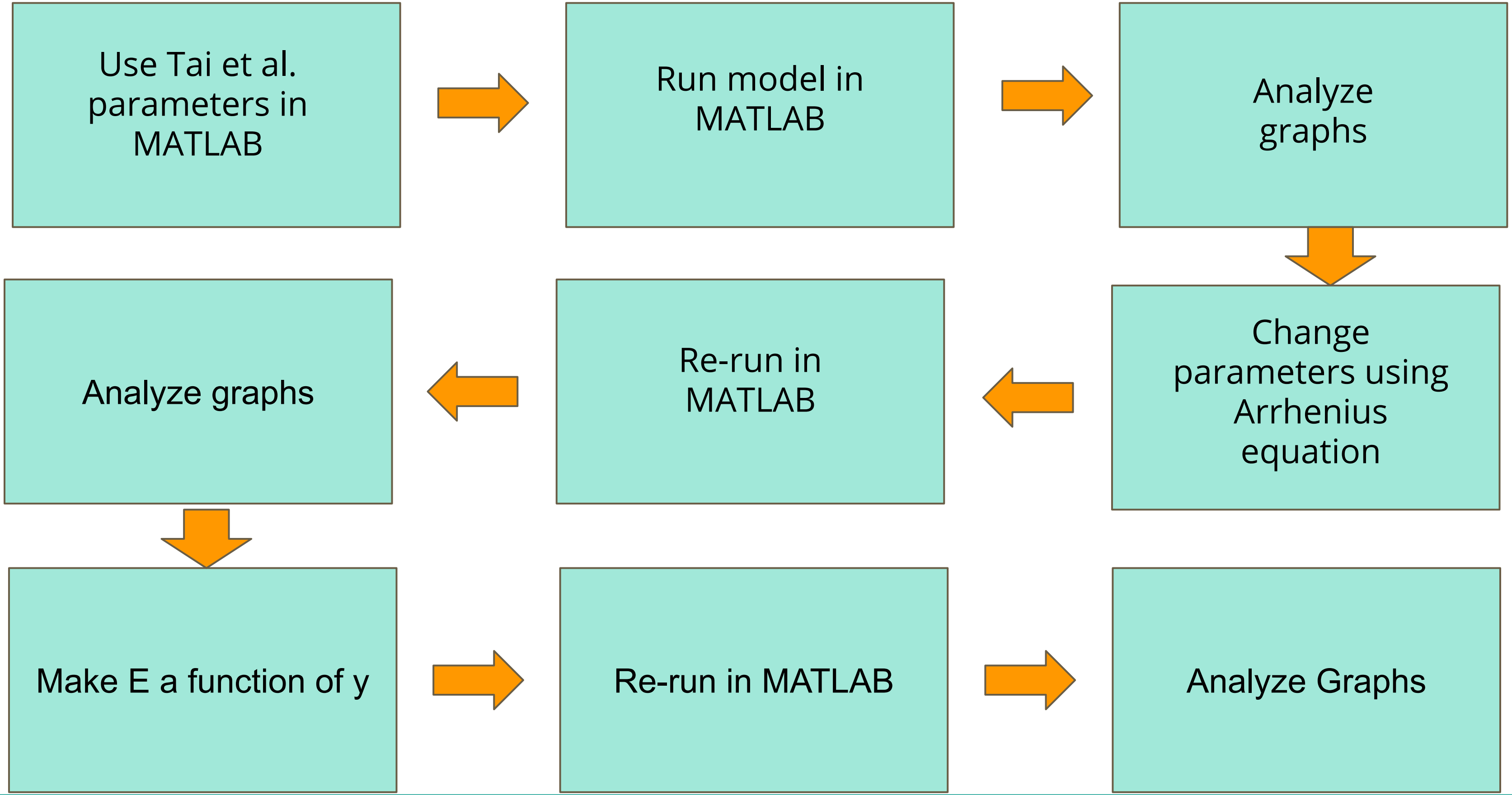
Outline

- Introduce known and expected yeast response to temperature
    - Methods and information from the literature
- Run the model and interpret resulting figures
    - First run with original parameters
    - Second run adjusting glucose efficiency
    - Third run with different rate constants based on temperature
- Discuss results and future directions
    - Comparison of three model runs and effectiveness of model tweaks
    - In the future, hope to create more accurate and descriptive models

S. cerevisiae known to show various cellular responses to temperature changes

- Optimum temperature range for growth is between 25 and 35 degrees C
- Suboptimal temperatures slow down enzyme kinetics
  - Consequently slows down cellular processes such as growth phrase
- Chemostat can be used to control specific growth rate and limiting nutrients (Carbon or Nitrogen)
- Our model estimates the dynamics of nutrients and biomass within the chemostats until they reach steady-state
  - Tai et al. 2007

Methods


Use Tai et al. parameters in MATLAB
Run model in MATLAB
Analyze graphs
Change parameters using Arrhenius equation
Re-run in MATLAB
Analyze graphs
Make E a function of y
Re-run in MATLAB
Analyze Graphs

Physiological characteristics of S. cerevisiae grown in ammonium- and glucose-limited anaerobic chemostat cultures Tai et al. (2007)

Table 1. Physiological characteristics of *S. cerevisiae* grown in ammonium- and glucose-limited anaerobic chemostat cultures

Limiting nutrient	Growth temperature (°C)	$Y_{Glu/X}$ ($g_{DW} \cdot g_{glucose}^{-1}$)	q_{Glu}[a]	q_{EtOH}[a]	q_{CO2}[a]	Carbon recovery (%)	Residual glucose (mM)	Residual ammonia (mM)
Glucose	12	0.07 ± 0.01	−2.5 ± 0.2	3.8 ± 0.3	4.4 ± 0.3	100 ± 3	2.8 ± 1.1	65.2 ± 2.2
Glucose	30	0.07 ± 0.00	−2.3 ± 0.0	3.5 ± 0.0	3.8 ± 0.2	95 ± 1	0.3 ± 0.1	61.3 ± 4.5
Ammonium	12	0.05 ± 0.00	−3.6 ± 0.2	6.1 ± 0.3	6.0 ± 0.6	97 ± 4	90.0 ± 9.8	1.5 ± 0.2
Ammonium	30	0.04 ± 0.00	−4.0 ± 0.1	6.8 ± 0.2	7.4 ± 0.2	97 ± 2	85.1 ± 8.2	0.2 ± 0.1

Cultures were grown at 30 and 12°C ($D = 0.03\ h^{-1}$). Values represent the mean ± SD of data from three independent steady-state chemostat cultivations. $Y_{Glu/X}$, biomass yield on glucose; DW, dry weight.

[a] Values expressed as $mmol \cdot g_{DW}^{-1} \cdot h^{-1}$.

Differential equations that represent the rates of change of biomass, glucose, and ammonium are used to see dynamics and find steady states

Each variable is in steady state when its differential equation is equal to zero.

- Biomass $$\frac{dx}{dt} = x\frac{ryz}{(y+K)(z+L)} - qx$$
- Glucose $$\frac{dy}{dt} = -Ex\frac{ryz}{(y+K)(z+L)} - qy + qu$$
- Ammonium $$\frac{dz}{dt} = -Fx\frac{ryz}{(y+K)(z+L)} - qz + qv$$

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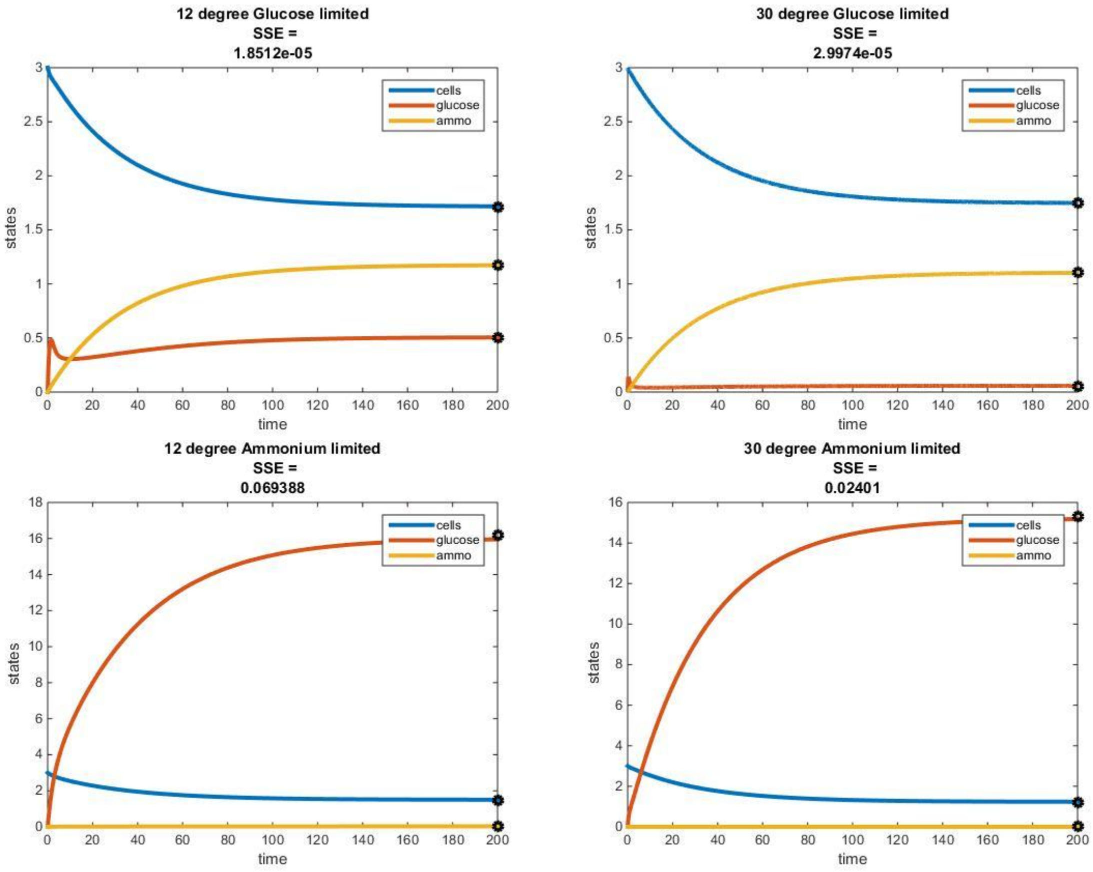
Models for all four conditions reach steady state by 200 hours



- Differences in biomass and nutrient dynamics vary most by limiting nutrient.

Steady-state biomass for each respective model

1.718 g	1.746 g
15.95 g	15.18 g

Glucose efficiency dependent on glucose levels and temperature

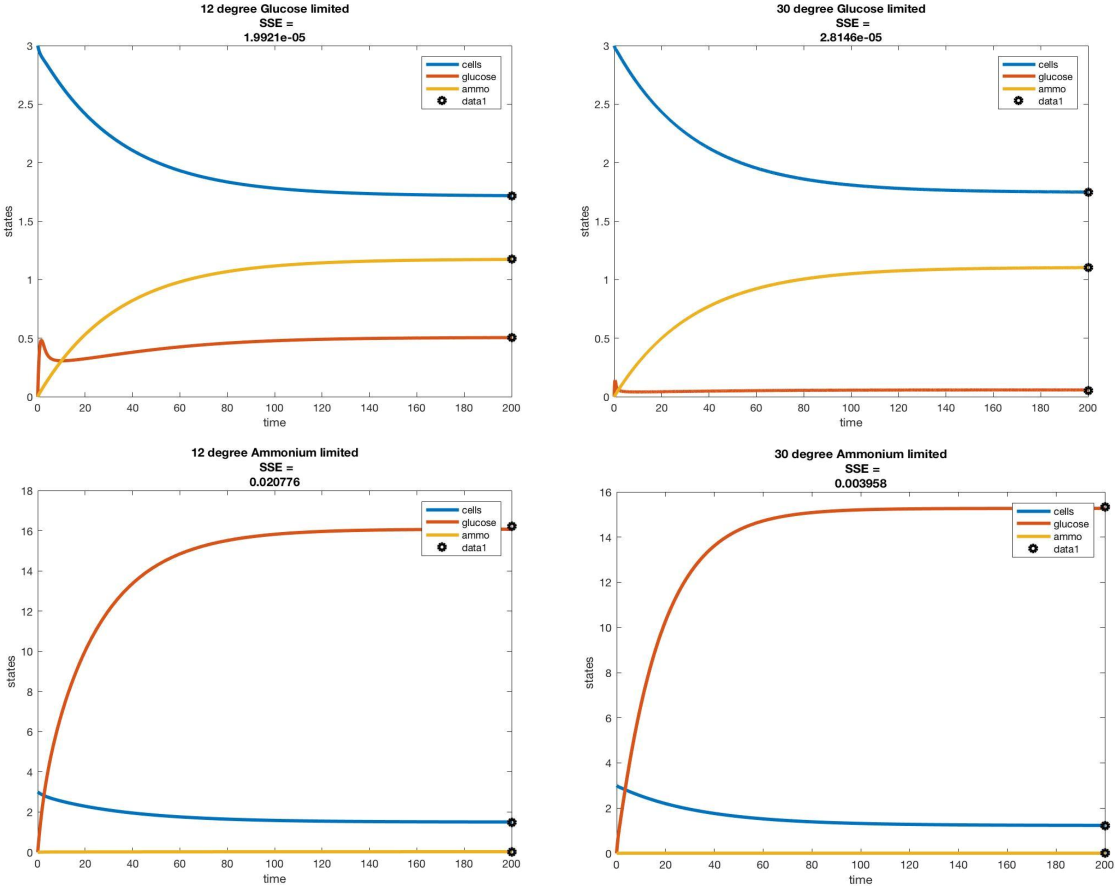
$$\frac{dy}{dt} = -Ex\frac{ryz}{(y+K)(z+L)} - qy + qu$$

- Linear equations for E at each temperature

$$E_{12} = 0.3637 * y + 14.1022$$

$$E_{30} = 0.7012 * y + 14.2478$$

Replacing E and rerunning the model produces similar results



- No noteworthy differences in graphs from original run
- E = 1/Y may be a good enough approximation

Temperature Effect using Arrhenius' Theory

- We want to predict what r can be at various temperatures
- Modeled by Arrhenius' Theory:

r = Ae^(-B/RT)

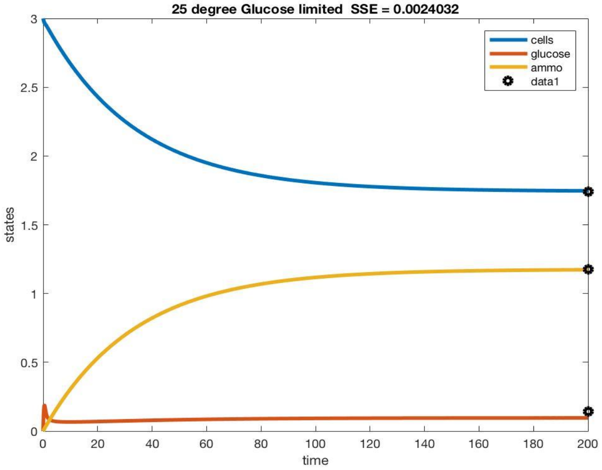
  - r = rate constant
    - See Table 2
  - A = orientation
    - 4.907*10^11
  - B = activation energy for the reaction
    - 68258.79
  - R = Universal Gas Constant
    - 8.3145 J/mol
  - T = Temperature in Kelvins
    - See Table 2

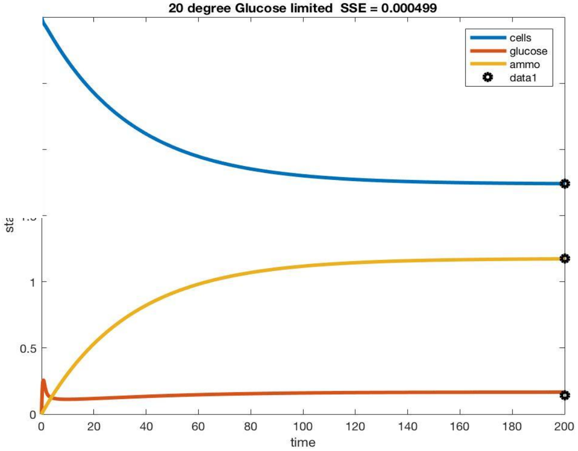
Observing the temperature effect using Arrhenius' equation

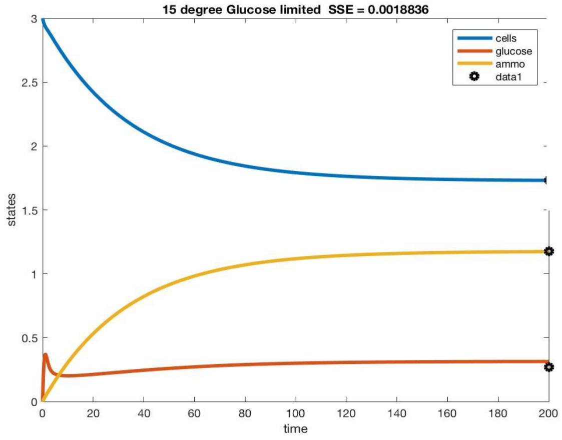
Table 2: This table depicts the rates that were calculated using Arrhenius' equation using the temperatures listed below

Temperature (°C)	12	15	20	25	30
rate	0.08	0.11	0.18	0.29	0.46

Temperature Effect Results







- Blue and yellow curves reached steady state in all three scenarios
- The 20℃ glucose limited was closest to reaching steady state with the parameters used
  - Modelled better (had smaller SSE value)

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Discussion and Future Directions

- Changing E and rerunning the model showed similar results in all graphs which suggests that E is a function of y
- As temperature increases, the rate increases
- Majority of the figures approached steady state, suggesting the parameters we used were good fits
- Future Directions
  - Test different parameters to see if we can get even better fits (some didn't reach steady state well)
  - Run for ammonium limited temperatures and compare with what we did

Conclusion

- Expected better fit model by making adjustments for temperature and glucose concentration
- Changed E and r parameters to see if more accurate
    - Created linear equations for E
    - Used Arrhenius equation to find r for any temperature
- Ran the models and did not see many differences from original
- Hope to continue to work on this model
    - Keep changing parameters and conditions

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