# Modeling the Conversion of Glucose to Fructose in Industry

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## Objectives

- Understand the mechanism by which glucose is converted to fructose.
- Use the Michaelis-Menten method to approximate and model the kinetics of the reaction.

## Introduction

Glucose and fructose are conformational isomers, which means that they have the same chemical formula ($C_6H_12O_6$), but the way in which these atoms are arranged gives them different properties as sugars. The conversion of glucose to fructose is an important reaction in the industrial synthesis of high fructose corn syrup (HSF). Glucose is the product of cellular respiration and is created by just about all living things.



Taking starches (of which glucose is the monomeric unit) and processing them to make HSF is a crucial part of the food industry, especially with the recent increase in foods containing HSF today [1]. The basic chemical principles behind this reaction involve enzyme-catalyzed isomerization from a six-membered glucose ring to a five-membered fructose ring (see Figure 1). Understanding the kinetics and equilibrium position of this reaction is essential to accomplish the goal of converting as much glucose to fructose as possible.
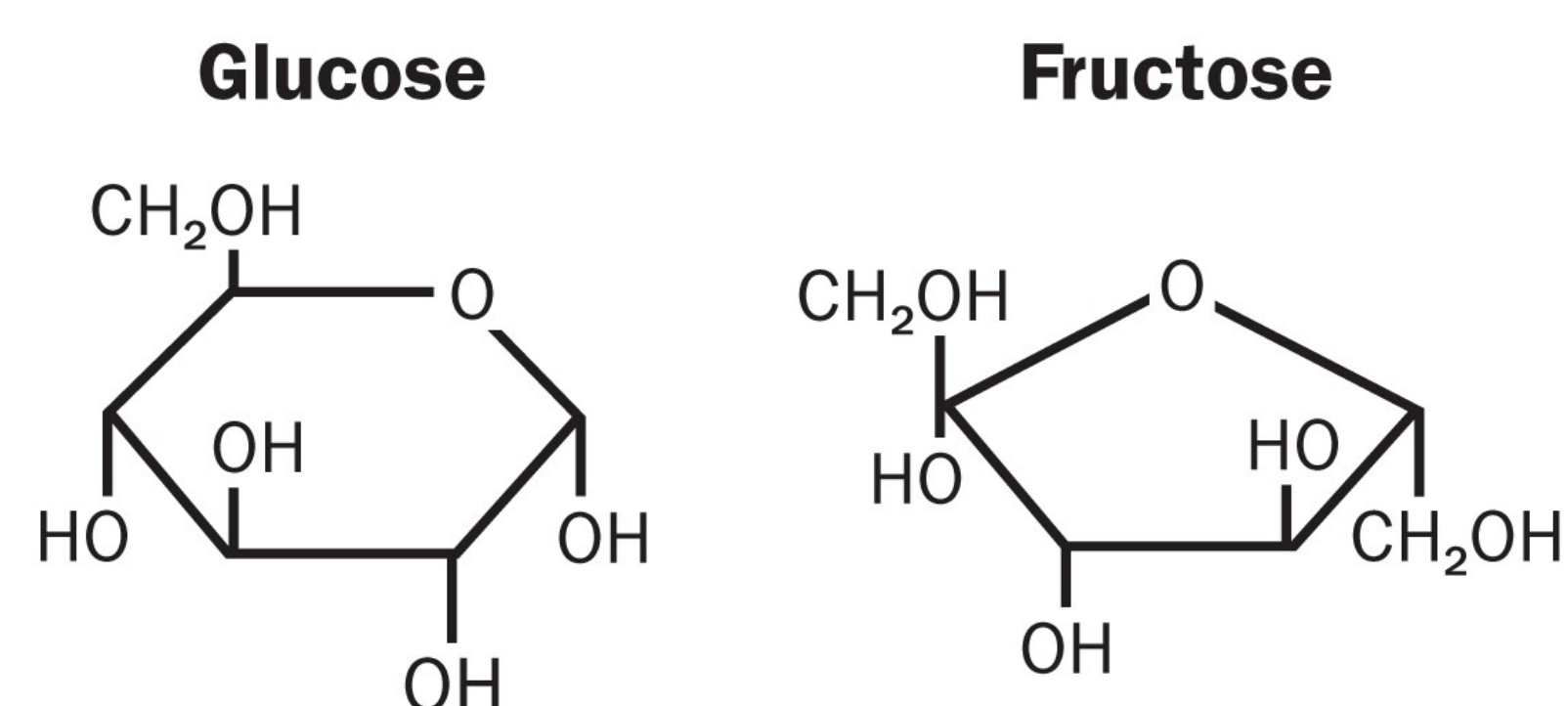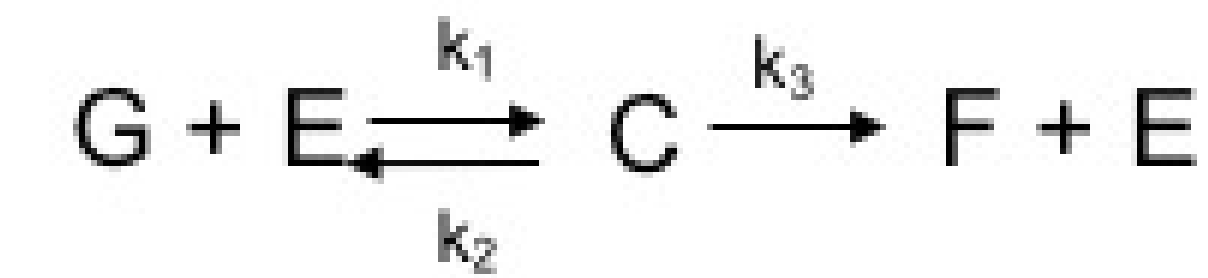


Figure 1: Molecular structure of glucose and fructose

## Modeling the Reaction

Let's assume the enzyme-catalyzed conversion of glucose to fructose takes place in a reaction of the following form:

$$G + E \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C \overset{k_3}{\rightarrow} F + E$$

Where G, E, and F represent the concentrations of glucose, isomerase enzyme, and fructose respectively. Now with initial conditions $G(0) = G_0$, $E(0) = E_0$, and $F(0) = C(0) = 0$ we write

$$\frac{dG}{dt} = -k_1 GE + k_2 C \quad (1)$$

$$\frac{dC}{dt} = k_1 GE - k_2 C - k_3 C \quad (2)$$

$$\frac{dE}{dt} = -k_1 GE + k_2 C + k_3 C \quad (3)$$

$$\frac{dF}{dt} = k_3 C \quad (4)$$

We can simplify this system of four equations to a system of two equations. Substituting $E = E_0 - C$ and simplifying, we have

$$\frac{dG}{dt} = -k_1 G(E_0 - C) + k_2 C \quad (5)$$

$$\frac{dC}{dt} = k_1 G(E_0 - C) - (k_2 + k_3)C \quad (6)$$

Non-dimensionalizing using $\gamma = G/G_0$, $\kappa = C/E_0$, and $\tau = tk_1 E_0$, we have initial conditions $\gamma(0) = 1$ and $\kappa(0) = 0$ and we write

$$\frac{d\gamma}{d\tau} = -\gamma + (\gamma + \frac{k_2}{k_1 G_0})\kappa \quad (7)$$

$$\frac{d\kappa}{d\tau} = \frac{G_0}{E_0}\gamma - (\frac{G_0}{E_0}\gamma + \frac{k_2 + k_3}{k_1 E_0})\kappa \quad (8)$$

Now, assuming $G_0 >> E_0$ (i.e. there is far more glucose than enzyme), we can substitute $\epsilon = E_0/G_0$ so that $\epsilon << 1$. Now substituting $\lambda = \frac{k_2}{k_1 G_0}$ and $\mu = \frac{k_2 + k_3}{k_1 G_0}$ we rewrite (7) and (8) as

$$\frac{d\gamma}{d\tau} = -\gamma + (\gamma + \lambda)\kappa \quad (9)$$

$$\epsilon\frac{d\kappa}{d\tau} = \gamma - (\gamma + \mu)\kappa \quad (10)$$

## Approximating the Solution

We can now apply singular perturbation methods to this system. For the outer approximation, we set $\epsilon = 0$ to obtain

$$\kappa_o = \frac{\gamma_o}{\gamma_o + \mu} \quad (11)$$

from (10), which can then be substituted into an outer approximation of (9) to get

$$\frac{d\gamma_o}{d\tau} = -\frac{\mu - \lambda}{1 + \mu/\gamma_o} \quad (12)$$

and then integrated to obtain

$$\gamma_o + \mu ln\gamma_o = -(\mu - \lambda)\tau + K \quad (13)$$

For the inner approximation, we take $T = \frac{\tau}{\delta(\epsilon)}$, $Y(T) = \gamma(\tau)$, and $Z(T) = \kappa(\tau)$ to get

$$\frac{1}{\delta(\epsilon)}\frac{dY}{dT} = -Y + (Y + \lambda)Z \quad (14)$$

$$\frac{\epsilon}{\delta(\epsilon)}\frac{dZ}{dT} = Y - (Y + \mu)Z \quad (15)$$

Choosing $\delta(\epsilon) = \epsilon$ and subsequently setting $\epsilon = 0$ gives us our inner approximation

$$\frac{dY_i}{dT} = 0 \quad (16)$$

$$\frac{dZ_i}{dT} = Y_i - (Y_i + \mu)Z_i \quad (17)$$

We'll ignore what happens with equations related to dC/dt from here on to focus on modeling the concentration of glucose. Integrating (16) we find that $Y_i(T)$ is constant, and applying $Y_i(0) = 1$ we get

$$Y_i(T) = 1 \quad (18)$$

Matching our inner and outer equations according to $\lim_{\tau \to 0} \gamma_o(\tau) = \lim T \to \infty Y_i(T)$ we get

$$\lim_{\tau \to 0}\gamma_o(\tau) + \mu \lim_{\tau \to 0} ln\gamma_o(\tau) = K \quad (19)$$

with intitial condition $\gamma(0) = 1$ this yields

$$1 + \mu ln(1) = K \quad (20)$$

Thus $K = 1$. The unified approximation $\gamma_u = \gamma_o + \gamma_i - (matching condition)$ thus becomes

$$\gamma_u + \mu ln(\gamma_u) = -(\mu - \lambda)\tau + 1 \quad (21)$$
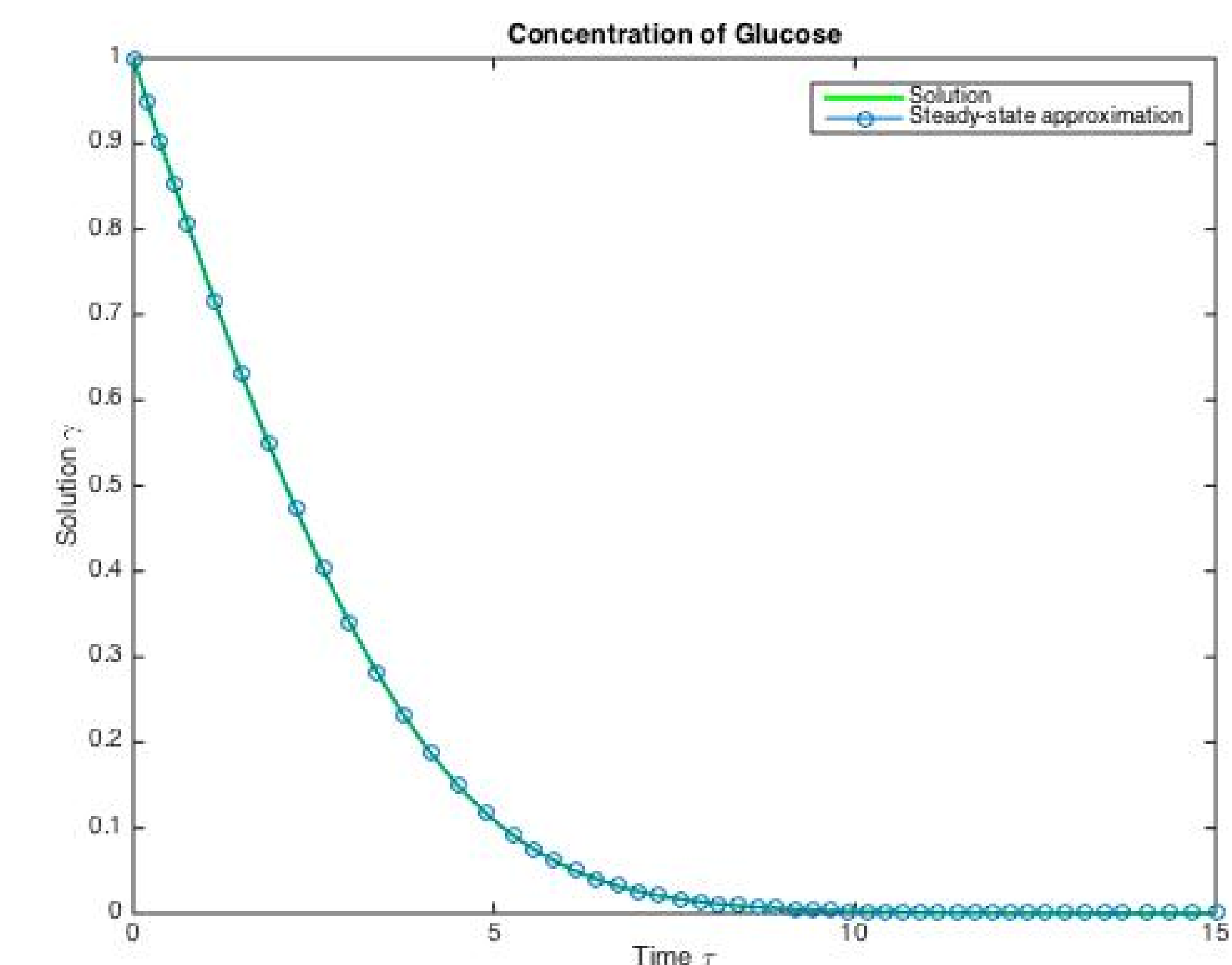
## The Michaelis Menten Equation

In light of the fact that $\gamma_u = \gamma_o$, the differential form of our final solution should look very similar to (12). And indeed if we multiply the right hand side of (12) by $\frac{\gamma}{\gamma}$ we obtain the famous Michaelis-Menten equation,

$$\frac{d\gamma}{d\tau} = -\frac{(\mu - \lambda)\gamma}{\mu + \gamma} \quad (22)$$

which hinges on the assumption of a quasi steady-state intermediate (i.e. that $\frac{d\kappa}{d\tau} = 0$) [2].

## Results

The plot of our steady state approximation for $\gamma(\tau)$ is shown below along with the numerical solution to the non-dimensionalized system (9) and (10). Values of $\mu$ and $\lambda$ were obtained using k-values from the literature, while epsilon was taken to be 0.01 for this example [3].



## Conclusion

The steady-state approximation fits very closely with the computational solution given by MATLAB's ode45. Literature suggests that, in reality, glucose and fructose achieve an equilibrium because the conversion of enzyme complex to fructose and enzyme is reversible [3]. Strategies for pushing this equilibrium towards the products side include running the reaction at 60 degrees Centigrade and continuously removing fructose from the reaction [3].

## References

1: Bray, George. http://ajcn.nutrition.org/content/79/4/537.full

2: Logan, J. D. *Applied Mathematics*. 2006.

3: Gaily, Mohamed. Isomerization and Kinetics of Glucose into Fructose. *International Journal of Engineering and Technology* 10:3. 2010.