ABE202 HW due Thursday april 20th.

The human body metabolizes ethanol into acetaldehyde in a reversible process using the enzyme Alcohol dehydrogenase (ADH). Acetaldehyde is metabolized in an irreversible process by the enzyme aldehyde dehydrogenase (ALDH).

A.

ethanol

$$CH_3CH_2OH + ADH \underset{NAD^+/NADH}{\leftrightarrow} CH_3CH_2OH \bullet ADH$$

$$CH_3CH_2OH \bullet ADH \underset{NAD^+/NADH}{\leftrightarrow} CH_3CHO \bullet ADH + H_2O$$

$$CH_3CHO \bullet ADH \leftrightarrow CH_3CHO + ADH$$

acetaldehyde

$$CH_3CHO + ALDH \underset{NAD^+/NADH}{\leftrightarrow} CH_3CHO \bullet ALDH$$

$$H_2O + CH_3CHO \bullet ALDH \underset{NAD^+/NADH}{\leftrightarrow} CH_3COOH \bullet ALDH$$

$$CH_3CHOOH \bullet ALDH \rightarrow CH_3COOH + ALDH$$

In class, we previously modeled a system of 2 ODEs from the Wilkerson paper which described the change over time in alcohol content of the intestine (dI/dt) and the body or blood (dB/dt). This system of ODEs can be modified to incorporate the effect of alcohol metabolism into acetaldehyde. Below we have begun this process for you. dI/dt is unchanged as no alcohol metabolism takes place in the intestine.

dB/dt is modified to reflect the amount of alcohol in body that is metablized into acetaldehyde.

A third ODE, dA/dt is added to reflect acetaldehyde concentration in the body over time.

$$\frac{dI}{dt} = K_e \left(\frac{FD}{V}\right) e^{-K_e t} - K_a I$$

$$\frac{dB}{dt} = K_a I - ?$$

$$\frac{dA}{dt} = ?$$

Net rate of metabolism of alcohol into acetaldehyde = $\left(\frac{V_{ADHmax} \times B - A \times V_{ADHrev}}{K_{M \cdot ADH} + B + A \times K_{ADHrev}}\right)$

Rate of clearance of acetaldehyde = $\left(\frac{V_{ALDHmax} \times A}{K_{M \cdot ALDH} + A}\right)$

Where I is alcohol in Intestine, B is alcohol in Body, A is Acetaldehyde in Body

Coefficients

$$K_e = \frac{K_{eMax}}{(1 + aD^2)}$$

K_{eMax} = 10.2 per hour
a = 0.00167 (1/g^2)
K_a=25.1 per hour
V=44.100 ml
V_m = 0.202 mg/mlxhr
K_m=0.0818;%mg/ml
V_{ADHmax}= .184;
$V_{ALDHmax}$= .246;
K_{ADHrev}= 1;
V_{ADHrev}= 3.26;
$K_{M \cdot ADH}$ = 0.014; %mg/ml
$K_{M \cdot ALDH}$ = 0.0000528; %mg/ml

Rev in the coefficient name means that that is the rate for the reverse reaction of ADH. Meaning that is the rate at which acetaldehyde turns back into alcohol.

F is 0.785 at D = 11.2 mg; F is 0.96 at D = 22.4 mg; F is 1 at D > 22.4 mg

Questions:

1) Give the full equations for dB/dt and dA/dt
2) Plot **alcohol and acetaldehyde** concentration for an individual who (inappropriately) consumes 8 standard shots of Vodka at 50% by volume Alcohol at once. What is the peak blood alcohol content and blood acetaldehyde content? How long after consumption does the peak blood alcohol level occur? When does the peak blood acetaldehyde level occur?
3) In the model how many drinks does it take to reach the Indiana legal limit for driving. (you can assume the drinks are all at once).
4) In class we have discussed the existence of heterozygous and homozygous mutants for ALDH. Heterozygous mutants have an ALDH that works at 70% of the wildtype rate. Homozygous mutants have an ALDH that works at 55% of the wildtype rate. Does this affect blood alcohol content in the mutants? What is the number of drinks to reach the legal limit for each genotype?

Bonus) 1 component of the chemical reactions (not ethanol) shown on page 1 is an ingredient in commercially available hangover 'cures'. Very briefly, which one and why?

Gibbs Free Energy Problems

8. Calculate ΔG°(25 °C) for K_{eq} = 0.001, 0.01, 0.1, 1, 10, 100, and 1000.

11. Which one of the following equations is used to evaluate free energy changes in cells under physiological conditions? What makes it appropriate?

(a) $\Delta G = RT \ln K_{eq}'$.

(b) $\Delta G = \Delta G^{\circ\prime} + RT \ln[\text{products}]/[\text{reactants}]$.

(c) $\Delta G = RT \ln[\text{products}]/[\text{reactants}]$.

(d) $\Delta G = \Delta H - T\Delta S$.

(e) $\Delta G = \Delta G^{\circ\prime} + RT\,[\text{products}]/[\text{reactants}]$.

Please submit these answers + graph + printout of code at the BEGINNING of class next Thursday (4/20).