Supporting Information

Middle Molecule Uremic Toxin Removal via Hemodialysis Augmented with an Immunosorbent Packed Bed

Shu Xia[1], *Nichole Hodge*[1], *Melvin Laski*[2], *and Theodore F. Wiesner*[1]

[1]Department of Chemical Engineering, Texas Tech University, Lubbock, TX 79409-3121

[2]Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX 79430

Corresponding author e-mail address: Ted.Wiesner@ttu.edu.

Static Experiments.

A static (no-flow) experiment was implemented in a 96-well plate prior to the flow experiment for two reasons: the first to investigate whether non-specific adsorption is sufficient to reduce PTH level to normal, and the second to verify if beads coated with monoclonal antibody adsorb significantly more protein than those without the antibody. The temperature of buffer was increased to body temperature by placing it in an incubator at 37 ˚C. Then PTH was put into buffer to a concentration of approximately 1000 pg/mL. Temporal concentration profiles of PTH for three types of solutions containing no beads, non-functionalized beads, and functionalized beads were measured.

The static experimental results are showed in Figure 1. Three curves are presented corresponding to a homogenous solution of PTH, the PTH solution in the presence of non-functionalized beads, and the PTH solution in the presence of beads functionalized with antibodies against PTH. The PTH concentration declines for all three scenarios. The decline in the homogenous solution indicates that PTH is unstable in buffer at body temperature, degrading approximately 40% from 1100 pg /mL to 600 pg /mL over 5 hours. This degradation must be accounted for when assessing the amount of the hormone adsorbed by the sorbent. The middle curve indicates that adding non-functionalized beads results in slightly more PTH removal via non-specific adsorption. The bottom curve indicates that specific adsorption associated with high-affinity binding between PTH and its antibody significantly increases hormone removal.

Mathematical Model

The idealized process of patient plus extracorporeal circuit is illustrated in Figure 2. Please refer to Table 1 through Table 5 for symbol definitions and values.

Model Formulation

The extracellular compartment of the patient is modeled as a continuous stirred tank, in which the solute concentration is considered uniform. A solute balance in the extravascular compartment, which neglects the change in compartment volume due to dialysis, yields equation (1).

$$V_b \frac{dC_b}{dt} = GV_b - k_u C_b V_b \tag{1}$$

C_b is the concentration of PTH in theextravascular compartment. The volume of the extracellular compartment, V_b, is assumed to consist of the intravascular plasma as well as the interstitial fluid. The quantity G is the solute generation rate per unit volume of the extracellular compartment. k_u, is the value of the rate constant for endogenous clearance by the kidney and liver. The initial solute concentration in the extracellular compartment was set by experimental or literature conditions.

The dialyzer is modeled as a steady state countercurrent apparatus using the standard formulation described by equations (2) to (5)[1].

$$C_{HD} = (1 - E_{HD})C_{HP} \tag{2}$$

$$E_{HD} = \frac{K_{HD}}{Q_B} \tag{3}$$

$$\frac{K_{HD}}{Q_B} = \frac{\exp\left[\frac{K_0 A_m}{Q_B}\left(1 - \frac{Q_B}{Q_D}\right)\right] - 1}{\exp\left[\frac{K_0 A_m}{Q_B}\left(1 - \frac{Q_B}{Q_D}\right)\right] - \frac{Q_B}{Q_D}}, \qquad \frac{Q_B}{Q_D} \neq 1 \tag{4}$$

$$\frac{K_{HD}}{Q_B} = \frac{\frac{K_0 A_m}{Q_B}}{\frac{K_0 A_m}{Q_B} + 1}, \qquad \frac{Q_B}{Q_D} = 1 \tag{5}$$

The quantities C_{HD} and C_{HP} are the solute concentrations of the perfusate exiting the hemodialyzer and the hemoperfuser respectively. The quantity E_{HD} is the extraction fraction of solute from the blood, which is in turn related to the clearance of solute, K_{HD}, by equation (3). The clearance of PTH in the dialyzer by all mechanisms (dialysis, non-specific adsorption, and degradation) is described by equations (4) and (5), which is clinically insufficient in the case of a middle molecule.

After the earlier work by Lee et al.[2], we model the adsorber as a chromatographic column with equation (6).

$$\frac{\partial C}{\partial t} + u\frac{\partial C}{\partial z} + \nu\frac{\partial q}{\partial t} = -k_d C \tag{6}$$

Because the degradation of the solute may be significant *in vitro*, it should be included in the models. Hence, the model for the concentration of solute in the adsorber fluid phase is modified by including a degradation term on the right hand side of equation (6). Here k_d is the solute first order degradation constant. The adsorber solute balance has the following initial and boundary conditions.

$$\begin{aligned} &C(z,0) = 0 \\ &C(0,t) = C_b(t) \\ &C(0,0) = C_b(0) = C_{i0} \end{aligned} \tag{7}$$

The solute concentration on the adsorbent is commonly modeled as in equation (8).

$$(1-\varepsilon)\frac{dq}{dt} = k_c a_v (C - C_{eq}) \tag{8}$$

ε is the column porosity, k_c is the mass transfer coefficient, and a_v is the specific area of adsorbent per unit column volume. C_{eq} is the liquid phase concentration of PTH in equilibrium with the concentration in the solid.

Receptor-ligand affinities vary from 10^6 M^{-1} to 10^{12} M^{-1}. For our PTH-antibody complex, the affinity constant $K_A = 2\times10^{10}$ M^{-1}, near the high affinity end[3]. When the affinity of the sorbate to sorbent is very high, as in the case of antigens and their corresponding antibodies, the liquid-phase solute concentration in equilibrium with the solid is small. Thus we may approximately describe the solid phase solute concentration by setting C_{eq} in equation (8) to zero.

$$\frac{dq}{dt} = \frac{k_c a_v}{1-\varepsilon} C \tag{9}$$

Employing equation (1), the model for the extracellular compartment is

$$V_b \frac{dC_b}{dt} = GV_b - k_u C_b V_b + Q_B (C_{HD} - C_b) \tag{10}$$

Equation (2) relates the hemodialyzer output concentration to the input concentration of the solute. Putting equation (2) into equation (10) yields the coupling among the dialyzer, the hemoperfuser, and the extracellular compartment.

$$V_b \frac{dC_b}{dt} = Q_B (1 - E_{HD}) C_{HP} - (Q_B + k_u V_b) C_b + GV_b \tag{11}$$

We now introduce the dimensionless variables c_b=C_b/C_{b0} and $\tau = \overline{k_u} t$. $\overline{k_u}$ is the rate constant for endogenous solute removal in healthy persons. Therefore, model (11) becomes

$$\begin{aligned} &\frac{dc_b}{d\tau} = ac_{HP} - bc_b + \gamma \\ &c_b(0) = 1 \end{aligned} \tag{12}$$

$$\text{where } a = \frac{Q_B(1-E_{HD})}{\overline{k_u} V_b},\ b = \frac{Q_B + k_u V_b}{\overline{k_u} V_b},\ \gamma = \frac{G}{\overline{k_u} C_{b0}} \tag{13}$$

Putting equation (9) into equation (6) yields

$$\frac{\partial C}{\partial t} + u\frac{\partial C}{\partial z} + \left(\frac{k_c a_v}{1-\varepsilon}\nu + k_d\right) C = 0 \tag{14}$$

Letting $c = \frac{C}{C_{b0}}, x = \frac{\overline{k_u} z}{u}, \beta = \frac{\frac{k_c a_v}{1-\varepsilon}\nu + k_d}{\overline{k_u}}$, and $\alpha = \frac{\overline{k_u} L_{HP}}{u}$, we now non-dimensionalize equation (14) and its initial and boundary conditions such that:

$$\begin{gathered} \frac{\partial c}{\partial \tau} + \frac{\partial c}{\partial x} = -\beta c \\ c(x,0) = 0 \qquad 0 \le x \le \alpha \\ c(0,\tau) = c_b(\tau) \qquad \tau > 0 \\ c(0,0) = c_b(0) = 1 \end{gathered} \tag{15}$$

System (15) is a non-homogeneous kinematic wave equation, and has the following solution[4].

$$c(x,\tau) = c_b(x-\tau)e^{-\beta\tau} \quad \tau \le x \tag{16}$$

$$c(x,\tau) = c_b(\tau-x)e^{-\beta x} \quad \tau > x \tag{17}$$

Noting that $c_{HP}(\tau) \equiv c(\alpha,\tau)$, which in turn is zero when $\tau \le \alpha$, equation (12) adopts two different forms depending on whether the column has broken through.

$$\begin{gathered} \frac{dc_b(\tau)}{d\tau} = -bc_b(\tau) + \gamma \quad \tau \le \alpha \\ c_b(0) = 1 \end{gathered} \tag{18}$$

when $\tau \ge \alpha$,

$$\frac{dc_b(\tau)}{d\tau} = ae^{-\alpha\beta}c_b(\tau-\alpha) - bc_b(\tau) + \gamma \quad \tau > \alpha \tag{19}$$

Equation (19) is a first order, linear delay differential equation. When the delay, α, is very small compared to the duration of the adsorption period, we can set it to zero (to be justified shortly). Under this assumption, equation (19) and its initial condition may be simplified to:

$$\begin{gathered} \frac{dc_b(\tau)}{d\tau} = -\left(b - ae^{-\alpha\beta}\right)c_b(\tau) + \gamma, \quad 0 \le \tau \le \tau_d \\ c_b(0) = 1 \end{gathered} \tag{20}$$

Equation (20) is a simple first order, linear nonhomogeneous ordinary differential equation, whose solution is equation (21). It is valid for the duration of the dialysis session, $0 \le \tau \le \tau_d$. We shall call this solution the dialysis period solution, $c_d(\tau)$.

$$c_d(\tau) = \left(1 - \frac{\gamma}{b - ae^{-\alpha\beta}}\right) e^{-\left(b - ae^{-\alpha\beta}\right)\tau} + \frac{\gamma}{b - ae^{-\alpha\beta}} \tag{21}$$

Following cessation of dialysis, the solute dynamics follows the pharmacokinetics model (1), which when non-dimensionalized is the same as equation (18). Following dialysis, the initial condition is the solute concentration at the end of dialysis, $c_d(\tau_d)$, which can be obtained from equation (21). Thus the solute concentration in the interdialytic period (the recovery phase) is described by equation (22).

$$c_r(\tau) = \left[c_d(\tau_d) - \frac{\gamma}{b_r}\right] e^{-b_r(\tau - \tau_d)} + \frac{\gamma}{b_r} \tag{22}$$

In the forgoing equation, b_r is the value of the parameter b in the recovery phase, without the extracorporeal circuit, i.e. $Q_B=0$. The two parameters are compared below.

$$\begin{aligned} b &= \frac{Q_B + k_u V_b}{\overline{k_u} V_b} \\ b_r &= \frac{k_u}{\overline{\overline{k_u}}} \end{aligned} \tag{23}$$

Two important characteristics of the recovery phase are evident from equation (22). The extracorporeal circuit influences the recovery of solute only through the value of the solute concentration, $c_d(\tau_d)$, at the end of dialysis (i.e. the beginning of the recovery phase). The dynamics of recovery are governed by the endogenous generation and clearance of the solute (embodied in the parameters γ and b_r, respectively). In particular, the time constant of recovery is $\left(\overline{k_u} b_r\right)^{-1}$.

To summarize, the time course of the solute concentration from the onset of one dialysis session to the onset of the next dialysis session is given by the following.

$$c_b(\tau)=\begin{cases} c_d(\tau)=\left(1-\dfrac{\gamma}{b-ae^{-\alpha\beta}}\right)e^{-\left(b-ae^{-\alpha\beta}\right)\tau}+\dfrac{\gamma}{b-ae^{-\alpha\beta}}, & 0\le\tau\le\tau_d \\ c_r(\tau)=\left[c_d(\tau_d)-\dfrac{\gamma}{b_r}\right]e^{-b_r(\tau-\tau_d)}+\dfrac{\gamma}{b_r}, & \tau_d<\tau\le\tau_{\max} \end{cases} \tag{24}$$

The dimensionless time, τ_{max}, is the interval between the starts of successive dialysis sessions.

For sizing the adsorption cartridge, the quantity of adsorbed solute in the solid phase is also of interest. This quantity can be obtained by integrating equation (9). We first non-dimensionalize it.

$$\frac{d}{d\tau}n(x,\tau)=\eta\cdot c(x,\tau) \tag{25}$$

In (25), $n(x,\tau)=q(x,\tau)/q_{max}$, where q_{max} is the maximum capacity of the sorbent (pg/mL of column volume). It is the local fractional saturation of the sorbent. All constants are grouped in the coefficient η.

$$\eta=\frac{k_c a_v C_{b0}}{\overline{k_u}(1-\varepsilon)q_{\max}} \tag{26}$$

The concentration in the adsorber liquid phase is taken from equations (16) and (17). Assuming that the initial solute concentrations in both the liquid and solid phases of the adsorber are zero, we obtain the following differential equation and initial condition for the solid phase sorbent concentration.

$$\begin{aligned} &\frac{d}{d\tau}n(x,\tau)=\begin{cases}\eta\cdot c_d(\tau-x)e^{-\beta x}, & x<\tau\le\tau_d \\ 0, & \text{otherwise}\end{cases} \\ &n(x,0)=0 \end{aligned} \tag{27}$$

Employing the expression for blood solute concentration during dialysis, equation (21), for $c_d(\tau)$; integrating system (27) yields a complicated expression for solid phase saturation, which is nonetheless in closed form.

$$n(x,\tau)=\begin{cases}\eta e^{-\beta x}\cdot\left[\dfrac{e^{-ae^{-\alpha\beta}x+bx+\alpha\beta}\left(e^{ae^{-\alpha\beta}(b-1)\tau}-1\right)}{a-be^{\alpha\beta}}+\dfrac{e^{-ae^{-\alpha\beta}x+bx+2\alpha\beta-b\tau}\left(e^{ae^{-\alpha\beta}\tau}-e^{b\tau}\right)\cdot\gamma}{\left(a-be^{\alpha\beta}\right)^2}+\dfrac{\gamma\cdot\tau}{b-ae^{-\alpha\beta}}\right], & x<\tau\le\tau_d \\ 0, & \text{otherwise}\end{cases} \quad (28)$$

Estimation of Model Parameters

We modeled the degradation of the solute in buffer as a simple first order decay process. The decay constant, k_d, was estimated from the top curve in Figure 1 as 0.1226 hr^{-1} (R^2 = 0.95). The PTH reduction in the flow experiment without adsorbent and the value of the degradation constant k_d from the static experiment allows us to determine the overall mass transfer coefficient in our experimental apparatus, K_0. We return to equation (21), which in the absence of solute generation and adsorbent simplifies to equation (29).

$$c_d(\tau)=e^{-(b-a)\tau} \quad (29)$$

with $a=\dfrac{Q_B(1-E_{HD})}{\overline{k_u}V_b}$ and $b=\dfrac{Q_B+k_dV_b}{\overline{k_u}V_b}$. Fitting of equation (29) to the top curve in Figure 1 yields a clearance of PTH by the dialyzer of K_{HD} =0.015 mL/min, and a value of the dialyzer overall mass transfer coefficient of K_0 =1.15 x 10^{-6} cm/min.

Very important for scale-up purposes is an accurate estimate of the concentration-based mass transfer coefficient, k_c. We employed the well-established Chilton-Colburn analogy for a packed bed[5].

All the dimensioned parameters for the *in vitro* experiment are summarized in Table 1. These 23 parameters are reduced to 5 dimensionless parameters as defined in the section on mathematical modeling, and the values of which are listed in Table 2.

The dynamics of the solute during and after a blood purification session may be described through symbolic manipulations of equations (24), which are simple first order processes. It is useful to note that the characteristics of the added adsorber are collected entirely in the factor $e^{-\alpha\beta}$. More specifically, the exponent is the product of adsorber residence time and mass transfer efficiency.

$$\alpha\beta = \underbrace{\frac{L_{HP}}{u}}_{\text{residence time}} \left(\underbrace{\frac{k_c a_v}{1-\varepsilon}\nu}_{\text{mass transfer efficiency}} + k_d \right) \tag{30}$$

During the session, the solute concentration drops with time constant t_r.

$$t_r = \frac{1}{\overline{k_u}\left(b - ae^{-\alpha\beta}\right)} \tag{31}$$

The quantity $c_d(\tau)$ is the fractional reduction in solute level as function of time. The limiting steady state for the intradialytic period is obtained by taking the limit of $c_d(\tau)$ as dimensionless time goes to infinity.

$$c_{bss} = \lim_{\tau\to\infty} c_d\left(\tau\right) = \frac{\gamma}{b - ae^{-\alpha\beta}} \tag{32}$$

The limiting steady state for our clinical scenario is C_{bss} =75 pg /mL. In view of the fact that the packed bed is far from saturation, the limiting steady state is established to balance the net PTH synthesis rate with its transport to the sorbent surface, i.e. the removal process is mass transfer limited. The time to approach within 1% of the limiting steady state is obtained by setting $c_d(\tau)$ equal to 1.01 c_{bss} and solving for τ.

$$\tau_{ss} = \frac{e^{\alpha\beta}}{b - ae^{\alpha\beta}} \ln\left[\frac{100\left(b - ae^{\alpha\beta}\right)\left(1 - \frac{\gamma}{b - ae^{-\alpha\beta}}\right)}{\gamma}\right] \tag{33}$$

For the clinical removal of PTH, it would require 4.5 hours to achieve this steady state, one hour longer than the average dialysis session. However, the PTH level drops only ~2 pg/mL from 3.5 hours to 4.5 hours, and extending the dialysis session to adsorb additional PTH would not be justified.

Literature Cited

(1) Fournier, R. L., *Basic Transport Phenomena in Biomedical Engineering*. Taylor and Francis: Philadelphia, PA, 1999.

(2) Lee, C. J.;Hsu, H. W.; Chang, Y. L. Performance Characteristics of Combined Haemodialysis/Haemoperfusionsystem for Removal of Blood Toxins. *Medical Engineering and Physics.* **1997,** *19,* 658.

(3) Lauffenburger, D. A. A.; Linderman, J. J. A., *Receptors : Models for Binding, Trafficking, and Signaling*. New York Oxford Univ. Press: 1993.

(4) Varma, A.; Morbidelli, M., *Mathematical Methods in Chemical Engineering*. Oxford University Press: New York, 1997.

(5) Skelland, A. H. P., *Diffusional Mass Transfer*. Robert E. Krieger Publishing Company: Malabar, FL, 1974.

(6) Momsen, G.; Schwarz, P. A Mathematical/Physiological Model of Parathyroid Hormone Secretion in Response to Blood-Ionized Calcium Lowering in Vivo. *Scand J Clin Lab Invest.* **1997,** *57,* 381.

(7) Pocotte, S. L.;Ehrenstein, G.; Fitzpatrick, L. A. Regulation of Parathyroid-Hormone Secretion. *Endocrine Reviews.* **1991,** *12,* 291.

(8) De Francisco, A. L.;Amado, J. A.;Prieto, M.;Alcalde, G.;Sanz de Castro, S.;Ruiz, J. C.;Morales, P.; Arias, M. Dialysis Membranes and PTH Changes During Hemodialysis in Patients with Secondary Hyperparathyroidism. *Nephron.* **1994,** *66,* 442.

(9) Habener, J. F.; Potts, J. T., Chemistry, Biosynthesis, Secretion, and Metabolism of Parathyroid Hormone. In *Handbook of Physiology*, American Physiological Society: Bethesda, MD, 1976; *Vol. 7-Endocrinology,* 313-342.

(10) Meyer, T. W.; Hostetter, T. H. Uremia. *New England Journal of Medicine.* **2007,** *357,* 1316.

(11) Ronco, C.;Ghezzi, P. M.;Morris, A.;Rosales, L.;Wang, E.;Zhu, F.;Metry, G.;De Simone, L.;Rhamati, S.;Adhikarla, R.;Bashir, A.;Manzoni, C.;Spittle, M.; Levin, N. W. Blood Flow Distribution in Sorbent Beds: Analysis of a New Sorbent Device for Hemoperfusion. *Int J Artif Organs.* **2000,** *23,* 125.

Tables

Table 1 Dimensioned parameters for Simulation of *In Vitro* Experiment

Parameter	Description	Value	Source
$\overline{k_u}$	rate constant for PTH clearance by liver and kidneys in healthy people	0.1098 min^{-1}	Table VI, Momsen et al.[6]
G	endogenous generation rate of PTH	0	experimental condition
k_u	rate constant for PTH clearance by liver and kidneys	0	experimental condition
V_b	volume of liquid compartment	2 liters	Chemostat size in experiment
M_{PTH}	molecular weight of PTH	9.5 kDa	Pocotte et al.[7]
D_{PTH}	diffusivity of PTH in water	1.5 x 10^{-6} cm^2/sec	Eq. 2-8, p. 27, Fournier[1]
k_d	rate constant for PTH degradation in water	2.0 x 10^{-3} min^{-1}	Experimental calculation
C_{b0}	initial concentration of PTH	1100 pg/mL	experimental condition, representative PTH level in patients with SHPT.
Q_B	circulation rate of liquid	65 mL/min	experimental condition
A_m	area for mass transfer in hemodialyzer	1.3 m^2	characteristic of Fresenius Optiflux F160NR hemodialyzer cartridge
V_{HD}	gross volume of dialyzer	216 mL	characteristic of Fresenius Optiflux F160NR hemodialyzer cartridge
K_o	overall mass transfer coefficient for PTH in dialyzer	1.15 x 10^{-6} cm/min	calculated from experiment in Defrancisco et al.[8].
K_{HD}	Clearance of PTH in hemodialyzer	0.015 mL/min	calculated from equation (4).

E_{HD}	extraction fraction of PTH in hemodialyzer	2.3 x 10^{-4}	calculated from equation (3)
u	interstitial velocity of liquid in adsorber	0.46 cm/sec	calculated from the relation $u = \frac{4Q_B}{\pi R_b^{\,2} \varepsilon}$
ε	porosity of adsorbent	0.48	experimental measurement of CNBr-activated Sepharose™ 4 Fast Flow adsorbent
$\nu = \frac{1-\varepsilon}{\varepsilon}$	ratio of solid volume to liquid volume in adsorber	1.083	calculated from porosity
R_b	radius of adsorption column	2.5 cm	characteristic of GE XK 50/20 column
L_{HP}	length of hemoperfuser	3 mm	experimental condition
d_p	adsorbent particle diameter	0.09 mm	experimental measurement of CNBr-activated Sepharose™ 4 Fast Flow adsorbent
a_v	specific area per unit volume of adsorbent	347 cm^2/cm^3	calculated assuming a packed bed of spheres
μ	viscosity of water	1 cP	physical property
ρ	density of water	1 gm/mL	physical property
k_c	liquid film mass transfer coefficient in packed bed	4.15 x 10^{-3}cm/sec	calculated from Chilton-Colburn analogy, Chapter 6, Skelland[5]
q_{max}	maximum PTH capacity of sorbert	0.38 gm/mL of sorbent	Calculated from ligand density of CNBr-activated Sepharose™ 4 Fast Flow adsorbent

Table 2 Values of Dimensionless Parameters for Simulation of *In Vitro* Experiment

Dimensionless Parameter	Description	Value
$a = \frac{Q_B(1-E_{HD})}{\overline{k_u}V_b}$	ratio of hemodialyzer clearance to endogenous clearance	0.296
$b = \frac{Q_B + k_u V_b}{\overline{k_u}V_b}$	ratio of total clearance to endogenous clearance	0.296
$\alpha = \frac{\overline{k_u}L_{HP}}{u}$	dimensionless hemoperfuser length	1.194×10^{-3}
$\beta = \frac{\frac{k_c a_v}{1-\varepsilon}\nu + k_d}{\overline{k_u}}$	ratio of clearance in hemoperfuser to endogenous clearance	1.64×10^{3}
$\gamma = \frac{G}{\overline{k_u}C_{b0}}$	Dimensionless endogenous solute generation rate.	0

Table 3. Comparison of Dimensions of the Hemoperfuser Before and After Scale-Up

Dimension	In Vitro Experiment (Before Scale-Up)	Clinical Design (After Scale-Up)
radius, R_b	2.5 cm	3.2 cm
length, L_{HP}	0.3 cm	1.37 cm

Table 4. Dimensioned parameters for Clinical Prediction (where different from *in vitro* parameters in Table 1)

Parameter	Description	Value	Source
k_u	rate constant for PTH clearance by liver and kidneys in patients with SHPT	3.9 x 10^{-3} min^{-1}	adjusted for consistency with C_{b0} and parameters from Momsen and Schwarz[6]
V_b	volume of extracellular compartment	15 liters	p. 338, Habener[9]
G	endogenous generation rate of PTH per unit volume of extravascular compartment	1.687 pg mL^{-1} min^{-1}	calculated using parameters from Momsen and Schwarz[6]
D_{PTH}	diffusivity of PTH in blood	6.6 x 10^{-7} cm^2/sec	Eq. 6-6, p. 153, Fournier[1]
C_{b0}	initial concentration of PTH	432 pg/mL	Defrancisco et al.[8]
Q_B	circulation rate of blood	300 mL/min	Defrancisco et al.[8]
Q_D	circulation rate of dialysate	500 mL/min	Defrancisco et al.[8]
A_m	area for mass transfer in hemodialyzer	0.6 m^2	characteristic of Sorin HFT 0.6 dialyzer cartridge used in Defrancisco et al.[8].
K_{HD}	Clearance of PTH in hemodialyzer	20 mL/min	Defrancisco et al.[8].
E_{HD}	extraction fraction of PTH in hemodialyzer	0.067	calculated from equation (3)
t_d	length of dialysis session	3.5 hours	Meyer[10]
u_0	superficial velocity of blood in adsorber	0.62 cm/sec	Typical value for hemoperfusers, Table II, p. 128, Ronco et al.[11]
R_b	radius of adsorption column	3.2 cm	scaled up from experiment
L_{HP}	length of hemoperfuser	1.37 cm	scaled up from experiment
a_v	specific area per unit volume of adsorbent	347 cm^2/cm^3	calculated assuming a packed bed of spheres
μ	viscosity of blood	3 cP	p. 62, Fournier[1]
ρ	density of blood	1.056 gm/mL	p. 62, Fournier[1]
k_c	liquid film mass transfer coefficient in packed bed	3.39 x 10^{-3}cm/sec	calculated from Chilton-Colburn analogy, Chapter 6, Skelland[5]

Table 5 Values of dimensionless parameters for clinical prediction

Dimensionless Parameter	Description	Value
$a = \frac{Q_B(1-E_{HD})}{\overline{k_u}V_b}$	ratio of hemodialyzer clearance to endogenous clearance	0.17
$b = \frac{Q_B + k_u V_b}{\overline{k_u}V_b}$	ratio of total clearance to endogenous clearance	0.218
$\alpha = \frac{\overline{k_u}L_{HP}}{u}$	dimensionless hemoperfuser length	2.1×10^{-3}
$\beta = \frac{\frac{k_c a_v}{1-\varepsilon}\nu + k_d}{\overline{k_u}}$	ratio of clearance in hemoperfuser to endogenous clearance	1.34×10^{3}
$\gamma = \frac{G}{\overline{k_u}C_{b0}}$	Dimensionless endogenous solute generation rate.	0.036
η	dimensionless mass transfer coefficient defined by equation (26)	1.41×10^{-6}

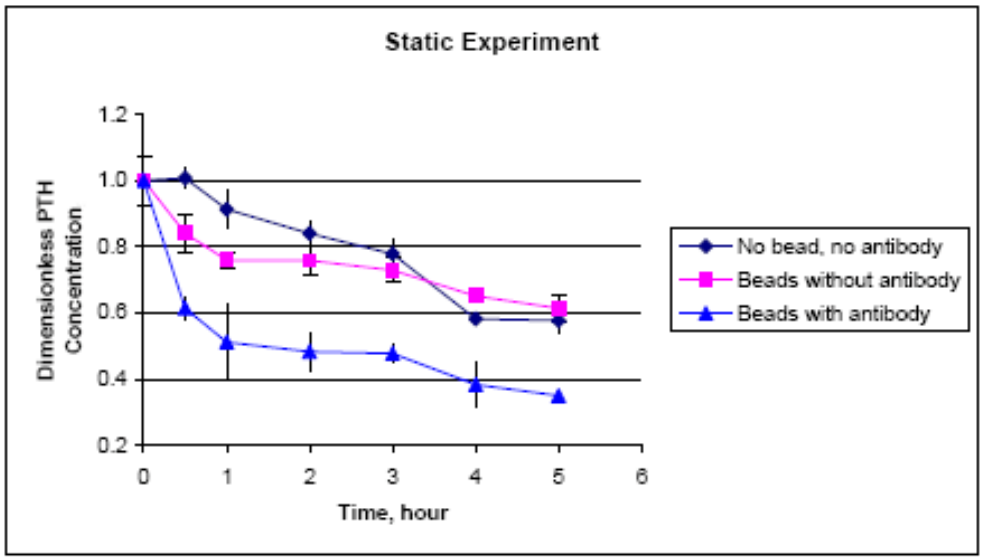

Figure 1. The results of static experiment for PTH solutions with no beads, non-functionalized beads and functionalized beads. Data are normalized to initial solute concentration. Error bars are ±SEM.

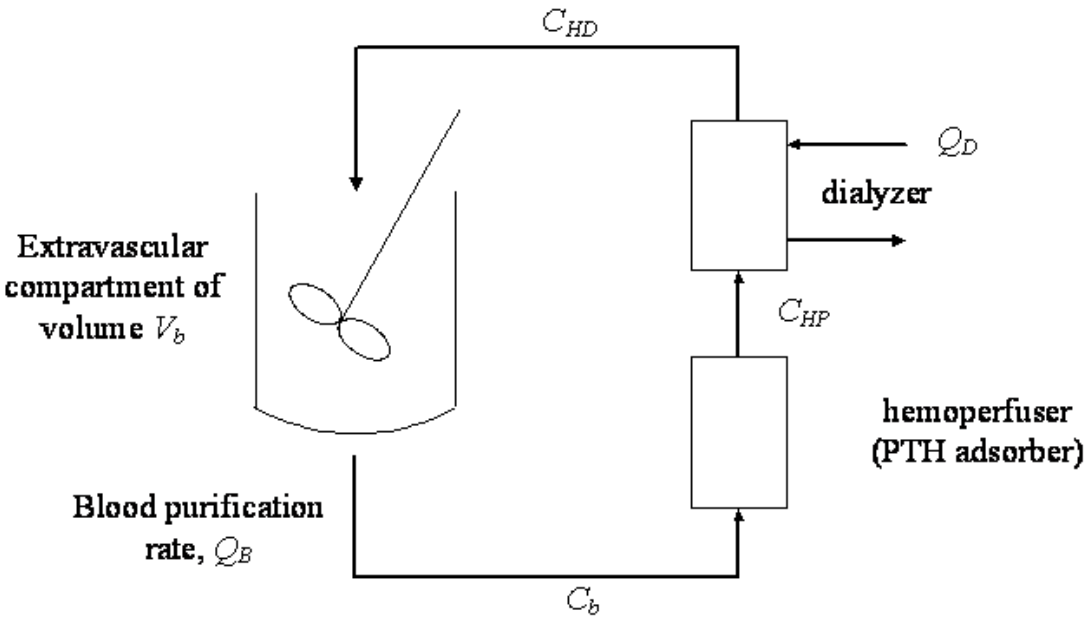

Figure 2. *In Vitro* Model of Combined Hemodialysis/Hemoperfusion System