# 링거액 주입시의 부피팽창 효과에 대한 모델링

# Modeling of Volume Expansion Effects During Infusion of Ringer's Solution

이 은 호, 최 규 택, 여 영 구*
(Eun Ho Lee, Kyu Taek Choi, and Yeong Koo Yeo)

**Abstract :** In this work the kinetics of volume changes of fluid spaces associated with infusion of Ringer's solution are analyzed using the body fluid space model. During infusion of Ringer's solution, the human body is assumed to be characterized by the fluid space model into which fluid is fed and from which fluid is left. Various infusion types were tested to accommodate different medical situations. Volunteers were given Ringer's solution and the changes in blood hemoglobin were detected. From the comparison with experimental data, the single- and two-fluid space models were found to represent adequately the kinetics of human volume expansion during infusion of Ringer's solution.

**Keywords :** volume expansion, Ringer's solution, Single-fluid space, Parameter estimation, Blood hemoglobin, Maximum dilution

## I. Introduction

Infusion of Ringer's solution(or Hartman's solution) is an important part of patient care in surgery or trauma care. It is well known that the amount of Ringer's solution needed to restore normal blood volumes is thought to be three to five times the volume of blood lost. The fluid molecules infused within the human body have been assumed to be distributed within a fluid spaceof constant volume. But it is obvious that volumes of fluid spaces change when a considerable amount of fluid is added or removed from the body. The volume expansion effect of the administered fluid is believed to be the therapeutic goal. However, this volume effect is difficult to study. Major differences in volume expansion between infusion fluids are fairly well known, but there is a lack of methods that represent their dynamic properties [1,2]. A water molecule entering the fluid space consisting of one expandable portion and one rigid portion can be found anywhere and therefore has a volume of distribution, being the sum of the two portions of the entire fluid space. But only the expandable portion of the fluid space is influenced by added water molecules. The volume effect of Ringer's solution has a time course that determines the optimal rate of infusion for the fluid. The blood volume is expanded most during and just after the infusion, but the expansion becomes less pronounced with time.

Recently fluid space volume models have been proposed and tested experimentally [3-5]. Stahle *et al.*[6] proposed an elementary mathematical models to represent the changes in volume of fluid spaces associated with intravenous administration of a crystalloid solution. They employed experimental results to estimated model parameters but failed to show the effectiveness of the proposed models upon which our study is based. Svensen and Hahn[7] analyzed volume kinetics of Ringer's solution, Dextran 70 and Hypertonic saline in male volunteers. They confirmed that the distribution of intravenous fluids can be analyzed by a kinetic model adapted for fluid spaces even with slightly different results depending on the marker used to indicate dilution of the primary fluid space. Volume kinetics of glucose solutions given by intravenous infusion were also analyzed by Sjostrand *et al.*[8].

In all the volume expansion models proposed so far the infusion was assumed to be represented as a block pulse. But, in some critical situations such as emergent surgery, infusion of Ringer's solution can be represented as a step or an impulse function. The purpose of the present study is to develop clear description on volume expansion caused by various types of infusion of Ringer's solution. Inthis study, we have worked with kinetic models that allow various types of infusion and can be applicable during and after volume loading.

## II. Single-fluid Space Model

The single-fluid space model can be considered as a balloon filled with water as shown in Fig. 1. During infusion, Ringer's solution enters an expandable fluid space of volume $v$ at a rate $k_i$ and is distributed in an expandable space. The functional form of $k_i$ is dependent upon the type of infusion. Typically $k_i$ can be block pulse, step, or impulse. The expandable fluid space has a target volume $V$, which the human body strives to maintain. The time-dependent volume $v$ changes due to the effluence of fluid from the fluid space by perspiration, basal diuresis and controlled

* 책임저자(Corresponding Author)
논문접수 : 2005. 0. 23., 채택확정 : 2006. 0. 29.
이은호, 여영구 : 한양대학교 화학공학과
(hanguk95@hotmail.com/ykyeo@hanyang.ac.kr)
최규택 : 울산대학교 서울아산병원 마취통증의학과
(olympic@nahana.net)

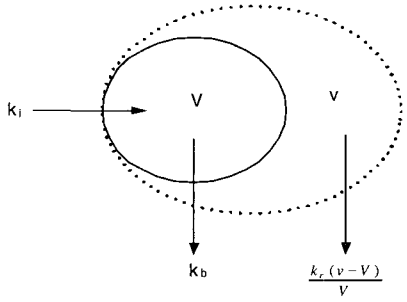



그림 1. 단일유체공간모델의 모식도.

Fig. 1. Schematic diagram of the single-fluid space model.

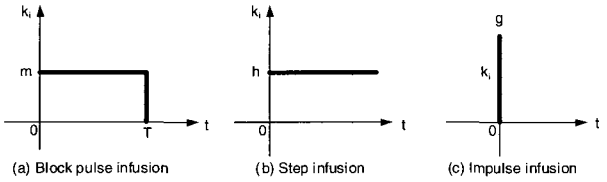



그림 2. 세 가지 주입형태.

Fig. 2. Three types of infusion.

efflux. The combined rate of fluid elimination due to perspiration and diuresis is represented as $k_b$. It is assumed that controlled efflux is proportional to the relative deviation of $v$ from the target volume V with the proportional constant $k_r$.

The behavior of the expandable volume can be represented by the following simple differential equation.

$$\frac{dv}{dt}=k_i-k_b-\frac{k_r(v-V)}{V},\ v(0)=V \tag{1}$$

We assume that $V$ and $k_r$ are constant. We now introduce the dilution at time $t$ as $u=\frac{v(t)-V}{V}$. Then we have $u(0)=0$, $dv=Vdu$. Equation (1) can be rewritten as

$$\left(\frac{V}{k_r}\right)\frac{du}{dt}=\frac{k_i}{k_r}-\frac{k_b}{k_r}-u \tag{2}$$

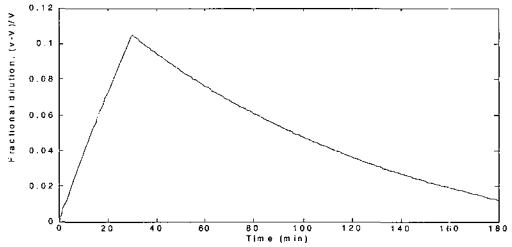
From the basal fluid loss the parameter $k_b$ can be estimated without much difficulty and the parameter $k_i$ can be controlled experimentally. Therefore these two parameters can be assumed to be known in the computation of model equations. Especially the parameter $k_i$ denotes the type of fluid infusion and we now consider three typical types as shown in Fig. 2. block pulse, step and impulse.

In most cases the parameters $k_b$ and $k_i$ in model equations are known as stated before. $u$ or $u_1$ is the measured dilution of blood and is available from experimental data. The remaining model parameters $k_r$, $k_t$ and two target volumes $V_1$ and $V_2$ should be estimated from the experimental data. In order to check first the effectiveness of the model equations developed in the present

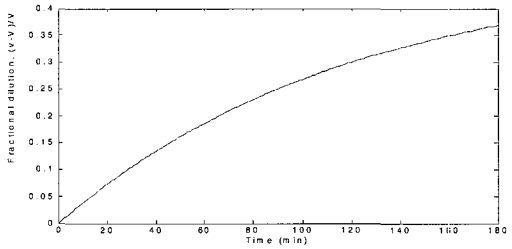
표 1. 수치모사에 사용된 모델 파라미터와 부피.

Table 1. Model parameters and volumes used in numerical simulations.

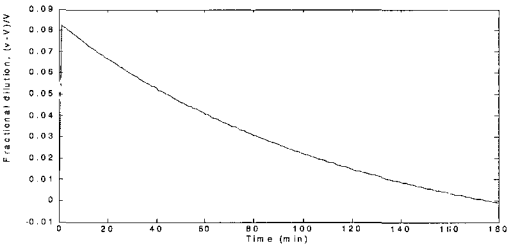
| Infusion type | T (min) | $k_b$ (ml/min) | $k_i$ (ml/min) | $k_r$ (ml/min) | $k_t$ (ml/min) | $V_1$ (liter) | $V_2$ (liter) |
|---|---|---|---|---|---|---|---|
| Block pulse | 30 | 2.5 | 50 | 100 | 200 | 4 | 8 |
| Step | - | 2.5 | 50 | 100 | 200 | 4 | 8 |
| Impulse | - | 2.5 | 1000 | 100 | 200 | 4 | 8 |




(a) Block pulse




(b) Step




(c) Impulse infusion

그림 3. 다양한 주입형태에 대한 모사결.

Fig. 3. Results of simulations for various infusion types.

study, we assume values of model parameters and target volumes as shown in Table 1 to perform numerical simulations. Simulations were performed using the MATLAB computing tool (version 7.0, MathWorks, U.S.A.). Fig. 3 shows results of simulations for block pulse infusion, step infusion and impulse infusion.

## III. Two-fluid Pace Model

The two-fluid space model can be considered as two balloons filled with water and connected each other as shown in Fig. 4. The primary fluid space communicates with a secondary fluid space. The net rate of fluid exchange between the expandable

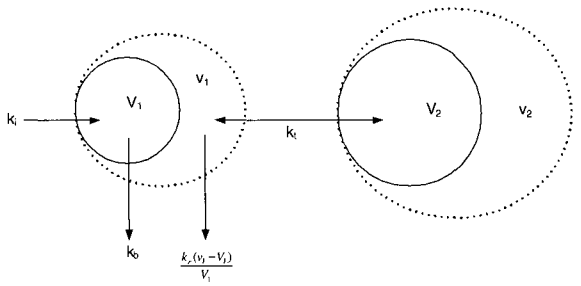



그림 4. 2-유체공간모델의 모식도.

Fig. 4. Schematic diagram of the two-fluid space model.

fluid spaces is proportional to the relative difference in deviation from the target volumes. The system strives to maintain the target volumes by acting on the controlled outflow mechanism in proportion to the relative deviation from the target volume of the primary fluid space.

During infusion, Ringer's solution enters an expandable fluid space of volume $v_1$ at a rate of $k_i$. As in the single-fluid space model, the functional form of $k_i$ can be block pulse, step, or impulse. There is a secondary expandable fluid space of volume $v_2$ which exchanges fluid with the primary fluid space $v_1$. Both fluid spaces have target volumes $V_1$ and $V_2$ respectively. $v_1$ changes with time due to the effluence of fluid from the fluid space by perspiration, basal diuresis and controlled efflux and due to the fluid exchange with the secondary fluid space. $v_2$ is time dependent due to the fluid exchange with the primary fluid space. The rate of fluid change between the two fluid spaces is assumed tobe proportional to the difference in relative deviations from the target volumes with the proportional constant of $k_t$. The combined rate of fluid effluence from $v_1$ due to perspiration and diuresis is represented as $k_b$. It is assumed that controlled efflux is proportional to the relative deviation of $v_1$ from the target volume $V_1$ with the proportional constant $k_r$. The behavior of the expandable volumes can be represented by the following differential equations.

$$\frac{dv_1}{dt}=k_i-k_b-\frac{k_r(v_1-V_1)}{V_1}-k_t\left(\frac{v_1-V_1}{V_1}-\frac{v_2-V_2}{V_2}\right) \quad (3)$$

$$\frac{dv_2}{dt}=k_t\left(\frac{v_1-V_1}{V_1}-\frac{v_2-V_2}{V_2}\right) \quad (4)$$

$$v_1(0)=V_1,\quad v_2(0)=V_2 \quad (5)$$

We assume that $V_1$, $V_2$, $k_r$ and $k_r$ are constant. As in the single-fluid space model, parameters $k_b$ and $k_i$ are considered to be known. Rearrangement of (3) and (4) gives

$$\left(\frac{V_1}{k_r+k_t}\right)\frac{du_1}{dt}=\frac{1}{k_r+k_t}(k_i-k_b)-u_1+\frac{k_t}{k_r+k_t}u_2 \quad (6)$$

$$\left(\frac{V_2}{k_t}\right)\frac{du_2}{dt}=u_1-u_2 \quad (7)$$

표 2. 수치모사 데이터.

Table 2. Data for numerical simulations.

| Infusion type | T (min) | $K_b$ (ml/min) | $K_i$ (ml/min) | $k_r$ (ml/min) | $K_t$ (ml/min) | $V_1$ (liter) | $V_2$ (liter) |
|---|---|---|---|---|---|---|---|
| Block pulse | 30 | 2.5 | 50 | 100 | 200 | 4 | 8 |
| Step | - | 2.5 | 50 | 100 | 200 | 4 | 8 |
| Impulse | - | 2.5 | 1000 | 100 | 200 | 4 | 8 |

where $u_1=\frac{v_1-V_1}{V_1}$, $u_2=\frac{v_2-V_2}{V_2}$.

We now consider three typical types as shown in Fig. 2. block pulse, step and impulse.

In most cases the parameters $k_b$ and $k_i$ in model equations are known as stated before. $u$ or $u_1$ is the measured dilution of blood and is available from experimental data. The remaining model parameters $k_r$, $k_t$ and two target volumes $V_1$ and $V_2$ should be estimated from the experimental data. In order to check first the effectiveness of the model equations developed in the present study, we assume values of model parameters and target volumes as shown in Table 2 to perform numerical simulations.

## IV. Experiments

Ringer's lactate solution was given to fourvolunteers. The ages and weights of volunteers are within the range of 28~34 years and 48~80kg respectively. The infusion experiments were approved by the Ethics Committee of Asan medical center in Seoul, Korea and each volunteer gave informed consent. Twelve hours before the experimental procedure, food and water were discontinued. Volunteers were placed comfortably on beds, and 20 minutes of equilibration was allowed before the fluid administration. Cannulae were placed into the antecubital vein and the radial artery. Ringers' lactate solution (Choong wae, Seoul, Korea), electrolyte contents of which were 130mmol/l of Na, 4mmol/l of K, 2mmol/l of Ca, 1mmol/l of Mg, 24mmol/l of lactate 24 and 110mmol/l of Cl. The Ringer's solution was infused into vein at a constant rate of 15ml/kg 30 min with the aid of infusion pumps (IVAC 560, San Diego).

Samples (1 ml each) for measurement of blood hemoglobin concentration were obtained from the radial arterial cannula at 0, 5, 10, 15, 20, 25, 30, 45, 60, 80, 100 and 120 minutes after administration. After a blood sample is drawn, 3ml of Ringer's solution isinjected to flush the cannula and one 2-ml sample to be discarded isdrawn before each blood sampling to avoid undue hemodilution caused by this fluid. Before infusion of the fluid, one sample is drawn in duplicate and the mean value is used in the calculations. Tables 3 shows experimental data represented as fractional dilutions obtained from infusion experiments.

Dilution occurring during intravenous infusion of Ringer's solution can be assumed to indicate an increase in the volume of

표 3. 블록펄스 주입에서의 상대편차 변화 (T=30min, kb = 1.94ml/min).

Table3. Changes of relative deviation in the block pulse infusion experiments (T = 30min, $k_b$ = 1.94ml/min).

| Time (min) | ID(volunteers) | | | | Average |
|---|---|---|---|---|---|
| | pch | lyj | pcw | ljy | |
| 0 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| 5 | 0.073 | 0.012 | 0.076 | 0.017 | 0.045 |
| 10 | 0.117 | 0.041 | 0.045 | 0.034 | 0.059 |
| 15 | 0.133 | 0.028 | 0.055 | 0.052 | 0.067 |
| 20 | 0.078 | 0.024 | 0.050 | 0.064 | 0.054 |
| 25 | 0.122 | 0.050 | 0.110 | 0.079 | 0.090 |
| 30 | 0.087 | 0.078 | 0.087 | 0.064 | 0.079 |
| 45 | 0.107 | 0.104 | 0.050 | 0.045 | 0.076 |
| 60 | 0.069 | 0.050 | 0.026 | 0.027 | 0.043 |
| 80 | 0.056 | 0.059 | 0.013 | 0.041 | 0.042 |
| 100 | 0.060 | 0.024 | 0.017 | 0.027 | 0.032 |
| 120 | 0.056 | 0.008 | 0.036 | 0.038 | 0.034 |
| Parameters | | | | | |
| Weight(kg) | 72 | 76 | 80 | 68 | 74 |
| Urine(ml)* | 750 | 400 | 600 | 190 | 485 |
| $k_b$ (ml/min) | 1.94 | 1.94 | 1.94 | 1.94 | 1.94 |
| T(min) | 30 | 30 | 30 | 30 | 30 |
| $k_i$ (ml/min) | 36 | 38 | 40 | 34 | 37 |

(* : Amount of urine collected after 120 minutes of infusion)

one or more expandable body fluid spaces. The volume of distribution is considered to be a constant. Similarly, the target volumes of the single- and two-volume models proposed in the present study are assumed to be constant, but the size of the fluid space expanded is changed. The size of a target volume can be found only by expanding the fluid space because it is the expandability that distinguishes this fluid space from other parts of the body water.

## V. Estimation of Model Parameters

The model parameters $k_r$, $k_t$ and target volume $V$ for the single- and two-fluid space model can be estimated from the experimental data shown in Table 3. Dilution occurring during intravenous infusion of Ringer's solution can be assumed to exhibit an increase in the volume of the expandable fluid space. We define function $f$ as following:

$$f = u(t) - \frac{m-b}{k_r}\left(1 - e^{-k_r t/V}\right) : 0 \le t < T \quad (8)$$

$$f = u(t) + \frac{b}{k_r} - \left[\frac{m}{k_r}e^{k_r T/V} - \frac{(m-b)}{k_r}\right]e^{-k_r t/V} : T \le t \quad (9)$$

Thus we can estimate parameters $k_r$, $k_t$, $V_1$, $V_2$ for the two volume model as follows:

표 4. 각 지원자에 대한 비례 파라미터와 부피 추정값.

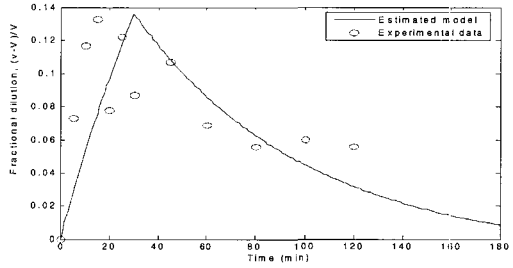
Table4. Estimated values of the proportional parameter and volume for each volunteer.

| Volunteers(ID) | $k_r$ (ml/min) | V(ml) |
|---|---|---|
| pch | 74.9 | 6,315 |
| lyj | 114 | 11,821 |
| pcw | 213.5 | 8,666.5 |
| ljy | 125 | 10,481 |
| Average | 119.9 | 8,969 |

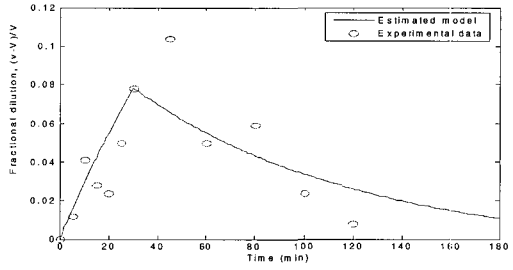
표 5. 추정결과(2-부피 모델).

Table5. Results of estimation (two-volume model).

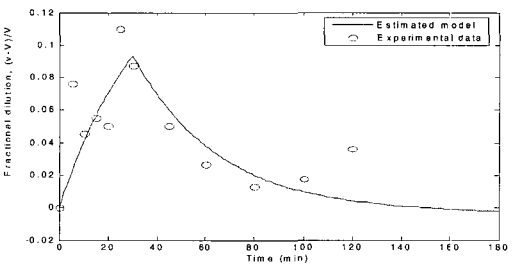
| Volunteers | $k_r$ (ml/min) | $k_t$ (ml/min) | $V_1$ (ml) | $V_2$ (ml) |
|---|---|---|---|---|
| pch | 45.5 | 399.2 | 1,358.6 | 6,212.5 |
| lyj | 126 | 67 | 7,745 | 10,079 |
| pcw | 173.9 | 85.2 | 6,900.4 | 8,474.5 |
| ljy | 64 | 286 | 6,654 | 12,973 |
| Average | 98.1 | 305.7 | 6,493.5 | 3,651.2 |




(a) pch



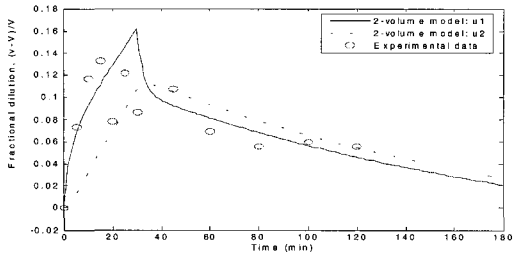

(b) lyj



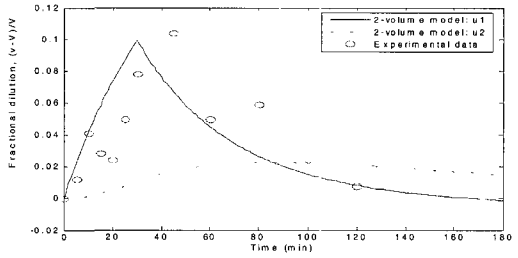

(c) pcw

그림 5. 단일유체공간모델에서의 부분희석도 실험값 비교.

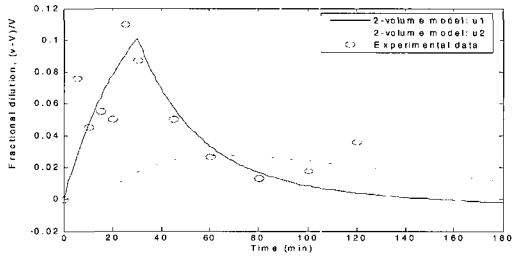
Fig. 5. Comparison between experimental values of fractional dilutions single-fluid space model.




(a) pch




(b) lyj




(c) pcw

그림 6. 2-유체공간모델에서의 부분희석도 실험값 비교.

Fig. 6. Comparison between experimental values of fractional dilutions for two-fluid space model.

$$f = u_1(t) - K\left(A_1 + B_1 e^{r_1 t} + C_1 e^{r_2 t}\right) : 0 \le t < T \tag{10}$$

$$f = u_1(t) + \left(\frac{KA_1 b}{m-b}\right) - KB_1 e^{r_1 t}\left\{1 - \left(\frac{m}{m-b}\right) e^{-r_1 T}\right\} - KC_1 e^{r_2 t}\left\{1 - \left(\frac{m}{m-b}\right) e^{-r_2 T}\right\}$$
$$: T \le t \tag{11}$$

Estimation of $k_r$ and $V$ can be performed from the minimization of $f$ based on experimental data given in Table 3. Table 4 and 5 show results of estimations for single- and two-fluid space models respectively.

In order to validate the fluid space model, the estimated parameters were plug into the model and results of computations were compared with experimental data. Fig. 5 shows results of comparison between experimental values of fractional dilutions and computational results of models based on the estimated parameters for three volunteers.

Certain volunteers show a little discrepancy between experimental results and simulation results but we can say that the single-fluid model show satisfactory tracking of overall trend of volume change for each volunteer. Characteristics of volunteers may be more distinguishable if we compare average values for volunteers[9].

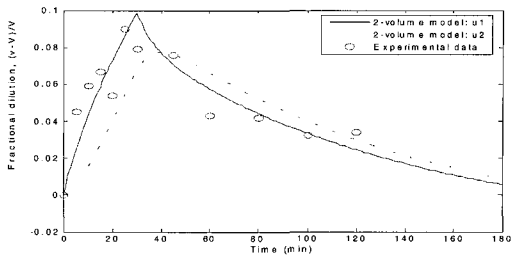



그림 7. 평균값에 근거한 부분희석도 실험값 비교.

Fig. 7. Comparison between experimental values of fractional dilutions based on average values.

Fig. 6 shows results of comparison between experimental values of fractional dilutions and computational results of single-volume models based on the estimated parameters for three volunteers. Fig. 7 shows results of comparison between average experimental fractional dilutions and computational results of models based on the estimated parameters using average experimental valuesfor two-fluid space model.It can easily be seen that two-fluid space model exhibits better performance in tracking experimental data.

## VI. Conclusions

Characteristics of volume expansion effect during infusion of Ringer's solution were analyzed using the single- and two-fluid space models. During infusion of Ringer's solution, the human body is assumed to be characterized by the single- and two-fluid space modelsinto which fluid is fed and from which fluid is left. The two-fluid space model has secondary volume space in addition to the first volume so that fluid exchanges between these two spaces are possible. Various infusion types were tested to accommodatedifferent medical situations. Volunteers were given Ringer's solution and the changes in blood hemoglobin were detected. From the comparison with experimental data, the single- and two-fluid space models were found to represent adequately the kinetics of human volume expansion during infusion of Ringer's solution.We can say that two-fluid space model exhibits better tracking performance compared to single-fluid space model. For identification of better models analysis of alternative candidates such as three-fluid space model and continuous space model is yet to be done.

## References

[1] F. Sjstrand, "Volume kinetics of glucose solutions given by intravenous infusion," *British Journal of Anaesthesia* 87 (6): 834-43, 2001.

[2] R. G. Hahn and M. D., Ph.D., "Kinetics of Isotomic and hypertonic plasma volume expanders," *Anesthesiology* 96: 1371-80, 2002.

[3] L. Stahle, A. Nilsson, and R. G. Hahn, "Modelling te

volume of expandable body fluid spaces during i.v. fluid therapoy," *British Journal of Anaesthesia* 78: 138-143, 1997.

[4] K. I. Brauer, M.D., "Volume kinetic analysis of the distribution of 0.9% saline in conscious versus Isoflurane-anesthetized sheep," *Anesthesiology* 96: 442-9, 2002.

[5] C. Svensen, M.D., "Volume kinetics of ringer solution, dextran 70, and hypertonic saline in male volunteers," *Anesthesiology* 87: 204-12, 1997.

[6] R. G. Hahn, D. Drobin, and L. Sthle, "Volume kinetics of Ringer's solution in female volunteers," *British Journal of Anaesthesia* 78: 144-148, 1997.

[7] R. G. Hahn and C. Svensn, "Plasma dilution and the rate of infusion of Ringer's solution," *British Journal of Anaesthesia* 79: 64-67, 1997.

[8] R. G. Hahn, M.D., Ph.D., "Volume kinetics of ringer's solution in hypovolemic volunteers," *Anesthesiology* 90: 81-91, 1999.

[9] R. G. Hahn, "Volume kinetics: a new approach fluid therapy," *Intensivmed* 37: 674-679, 2000.

[10] K. I. Brauer, M.D., "Volume kinetic analysis of the distribution of 0.9% saline in conscious versus Isoflurane-anesthetized sheep," *Anesthesiology* 96: 442-9, 2002.

**이 은 호**

2001년 2월 한양대 화공과. 2003년 2월 한양대 화공과(공학석사). 2003년~2005년 호남석유화학. 2006년 3월~현재 한양대 화공과 박사과정. 관심분야는 공정 모델링, 제어 및 최적화, 고분자공정의 제어.

**여 영 구**

1979년 8월 서울대 화공과 졸업. 1982년 2월 서울대 대학원 화공과 졸업(공학석사). 1986. 12월 Auburn대 대학원 화공과 졸업(공학박사). 1987년~1993년 KIST 선/책임연구원. 1993년~현재 한양대학교 응용화공생명공학부 교수. 관심분야는 공정 모델링, 제어 및 최적화, 공정인공지능.

**최 규 택**

1979년 8월 경북대 의예과 졸업. 1982년 2월 경북대 대학원 의예과 졸업(의학석사). 1985년 2월 경북대 대학원 의예과 졸업(의학박사). 1985년~1995년 계명대학교 교수. 1995년~현재 울산대 교수. 서울아산병원. 관심분야 마취에 따른 인체 감응변화, 수액투여모델.