Modelling of some aspects of a biomedical process: application to the treatment of digestive cancer (HIPEC)

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Abstract

Usual therapies against malignant tumors, such as surgery, chemotherapy, radiation, is severe and when repeated their efficiency may decrease because tumorous cells may become resistant. Contrarily, hyperthermia has been known for some time as an effective auxiliary treatment, which can be applied repeatedly. In some cases of abdominal carcinomatosis, particularly those of digestive origin, HIPEC is considered as an promising therapeutic option. Chemotherapy and hyperthermia are combined via the perfusion of the abdominal cavity with hot fluids containing chemotherapeutic agents, thus, augmenting the influence of appropriate chemotherapeutic agents with heat. The paper deals with in vivo temperature measurements during the treatment and the identification and development of a heat transfer model of the treatment and consequently its optimization. First, the focus is on in vivo acquisition and monitoring of temperatures. Temperature probe characteristics are identified. Next, a dynamic model for the heat transfer in the patient's body during the HIPEC is outlined. Then model is validated using experimental data collected by the medical partners (St-Etienne Bellevue and Lyon-Sud, France) during in vivo HIPEC. Finally, the concluding comments are reported, including the current perspectives. Since the effectiveness of HIPEC is based on the achievement of a uniform hyperthermic intracavity temperature, properly modelling and developing supervising/monitoring methods for heat transfer for this procedure is the motivation for this research. The paper presents some preliminary groundwork for an eventual simulator and decision aid related to HIPEC.

Keywords HIPEC · Heat transfer · Real-time temperature measurements · In vivo adaptative modelling

Introduction

The effectiveness of hyperthermia or thermotherapy in conjunction with other forms of cancer therapy has recently become well known. Research has demonstrated that high temperatures can injure and kill malignant cells, usually with minimal damage to healthy tissues (Vander Zee 2002) by exterminating cancer cells and damaging proteins and structures within cells (Hilderbrandt and Wust 2002), hyperthermia may diminish the size of tumors. This thermal chemical saturation of affected tissue allows better penetration the chemotherapeutic agents. In addition, this procedure

minimizes deleterious effects of high doses of intravenous chemotherapy.

The synergy of chemo-hyperthermia is even more compelling in the case when administered intraperitoneally for peritoneum carcinomatosis of digestive tract origin since these patients often die within 6 months. With heated or Hyperthermic Chemotherapy (HIPEC) there is a better assimilation of the chemotherapy locally in the peritoneal cavity, where systemic or traditional chemotherapy is known to be ineffective. This procedure, has become a very promising therapeutic option. HIPEC is applied during surgery, via an open or closed abdominal approach, the former in USA (Sugarbaker and Jablonsky 1995; Sugarbaker 1995), Germany (Jähne et al. 1997) and Japan (Yonemura et al. 1991) and the latter in France (Gilly et al. 1994; Salle et al. 1993; Detroz et al. 1994; Dubé et al. 1997).

Both have opposing advantages and drawbacks: temperature and drug homogeneity versus patient safety. This paper presents significant research results on the closed-abdomen HIPEC protocol, which seems inherently safer but is more

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Fig. 2 Cavitherm EFS 0685. **a** overall view. **b** In vivo operation: front display and control panel with a few measured values, diskette slot and RS232 connection. SUC: Single-use sterile integrated cartridge; with clot-traps, valves, pump, etc. Note only 2 temperature values out of eight measured can be displayed simultaneously

flow valves pump and heat generator, where output temperature is regulated in real-time.

Temperature is measured with the help of YSI 400-compatible thermistance sensors, which resistance R (in Ohm) varies with the temperature T (in °C). The corresponding $T=f(R)$ function is approximated by a 4th order polynomial, Eq. (1), which coefficient values are summed up in Table 1.

$$T = c_4 R^4 + c_3 R^3 + c_2 R^2 + c_1 R + c_0 \quad (1)$$

Therefore, the temperature acquisition device permanently performs the conversion between the measured resistance and the corresponding temperature. Moreover, the temperature measurements are affected by two important characteristics of the sensors and the measuring devices:

- Their resolution and accuracy,
- Dynamical (time response) parameters.

Temperature measurements

Dynamic parameters (time constants, delays) of the temperature sensors have been verified during different experiments, either in liquid or gaseous environments. Time constants thus experimentally determined were: $\tau_l \sim 6$ s in liquid and $\tau_g \sim 33$ s in gas (air). Time delays have been found negligible compared to the estimated time constants.

A time constant gives an idea of the rapidity of the convergence of the measured value from the real value, particularly in the case of a step-like variation of the latter, Fig. 3. It is admitted that the 95% of the final value of a step-response has been reached at 3τ . This applied to the estimated time constant values τ_l and τ_g gives 18 s and 99 s (= 1 min 39 s) respectively.

Let us stress the considerable slower response time lag if the sensor is operating in gaseous environment. In addition, air bubbles may be present in the abdominal cavity during IPHC. Therefore, it is of vital importance to have the temperature sensors correctly placed within the cavity; to be totally immersed and in contact with the organs which have to be monitored (liver, mesentery,...), since the manufacturer (www.ysitemperature.com) has provided the following thermistance sensor characteristics, within the considered temperature domain:

- Resolution: ± 0.1 °C, accuracy: ± 0.2 °C,
- Time constant: 6 s,

Fig. 3 Example of a first order response Y to a unitary step input U . Its time equation writes: $y(t) = K (1 - e^{-(t-T_d)/\tau})$

Table 1 Polynomial coefficient values for T (25, 55 °C)

T (°C)	c_4	c_3	c_2	c_1	c_0
Coefficient values					
[10; 15]	6.5×10^{-14}	-1.1×10^{-9}	8.7×10^{-6}	-3.4×10^{-2}	70,985
[15; 25]	-9.5×10^{-14}	7.4×10^{-10}	-7.2×10^{-8}	-1.6×10^{-2}	56,832
[25; 35]	6.5×10^{-13}	-6.4×10^{-9}	2.5×10^{-5}	-5.9×10^{-2}	83,754
[35; 45]	3.5×10^{-12}	-2.2×10^{-8}	6.1×10^{-5}	-9.4×10^{-2}	96,691
[45; 55]	1.9×10^{-11}	-8.4×10^{-8}	1.5×10^{-4}	-1.5×10^{-1}	11,102

Abdominal heat transfer model construction, identification and optimization

Abdominal heat transfer model construction

The effectiveness of IPHC is mainly on the achievement of a homogeneous hyperthermic intracavity temperature. The point is to reach this state so as to eliminate the tumorous cells without necrosing the healthy tissue. The general temperature objective is approximately 42 °C (315 °F).

During open-abdomen IPHC, a non-homogeneous temperature distribution can be corrected by simply “stirring” somewhat the abdominal organs. However with closed-abdominal IPHC, the possible corrective actions are much more limited, such as flow variations and/or flow inversions and have less impact on the outcome.

A model of the abdomen is being developed in order to understand the whole process better and to be able to optimize the procedure.

This will enable the simulation of the temperature evolution in the abdominal cavity versus input flow and temperature. Since the geometry of the abdominal cavity is rather complex, the initial modelling started with some simplified assumptions, such as:

- Liquid was likened to water,
- Abdominal cavity volume was approximated as a rectangular prism, Fig. 4,
- The output equaled input flow rate (steady state flow, no accumulation).

Fig. 4 Abdominal cavity after HIPE devices installation (Gilly medical team at CHLS, Lyon, FRANCE)

Variables and parameters for the heat transfer model

Let us now introduce the following variables and parameters, which are used in the proposed model, Table 2.

Heat transfer modelling

Total enthalpy balance applied to the liquid circulating in the patient's abdomen allows the following equation to be asserted:

$$V\rho_l C_l \frac{d\bar{T}}{dt} = \rho_l C_l Q(T_{in} - T_{out}) - S_e \Phi_{th} \quad (2)$$

with:

$$\Phi_{th} = h \cdot (\bar{T} - \bar{T}_p) \quad (3)$$

Since the considered process concerns heat transfer by forced convection, the following correlation function can then be considered:

$$Nu = f(R_e, P_r) \quad (4)$$

with (Welty et al. 2001) giving:

$$\begin{cases} Nu = \frac{h \cdot L}{k_{liq}} \\ R_e = \frac{\rho_l v D}{\mu_{liq}} \\ P_r = \frac{\mu_{liq} C_l}{k_{liq}} \end{cases} \quad (5)$$

The supposed geometrical form of the abdominal cavity (Fig. 4) as well as the nature of the liquid flow (supposed to be laminar) allows the function f giving the Nusselt's number (Bird et al. 2006) to be determined:

$$Nu = 0,664 \sqrt{R_e} \sqrt[3]{P_r} \quad (6)$$

therefore:

$$h = \frac{k_{liq} \cdot 0,664 \sqrt{R_e} \sqrt[3]{P_r}}{L} \quad (7)$$

The liquid flow velocity then is:

$$v(t) = \frac{Q}{S} \quad (8)$$

The temperature $\bar{T}$ usually denotes a logarithmic average of T_{in} and T_{out} . In this paper it has been simplified to a weighted mean:

$$\bar{T} = \alpha T_{in} + (1 - \alpha) T_{out} \quad (9)$$

Table 2 Heat transfer model

Parameter	Description
Q (m ³ /s)	The liquid circulation flow-rate in the patient's abdomen
ρ_l (kg/m ³)	Density of the liquid (supposed identical to water 1000)
C_l (J/kg)	Specific heat of the liquid (<i>idem</i> 4180)
S (m ²)	Flow's surface
S_e (m ²)	Heat exchange surface, between the liquid and the abdominal cavity
Φ_{th} (W/m ²)	Heat flow through the surface S_e
ν (m/s)	Average speed of the liquid circulating in the patient's abdomen
μ_{liq} (Pa·s)	Dynamic viscosity of the liquid (<i>idem</i> 0.66×10^{-3})
Nu	Nusselt's number
Re	Reynold's number
Pr	Prandtl's number
L (m)	Length of the patient's abdomen
l (m)	Width of the patient's abdomen
D (m)	Liquid layer thickness
h (Wm ⁻² K ⁻¹)	Heat transfer coefficient (<i>idem</i> 7.36)
k_{liq} (Wm ⁻¹ K ⁻¹)	Thermal conductivity (<i>idem</i> 0.60)
$\bar{T}$ (K)	Mean temperature of the liquid within the abdomen
$\bar{T}_p$ (K)	Mean temperature of the patient's body
T_{in} (K)	Input (inflow) temperature
T_{out} (K)	Output (outflow) temperature

with $0 < \alpha < 1$, It is supposed that:

$$S_e = \beta \cdot L \cdot l \quad (10)$$

where β is a fitting coefficient of the model relating the heat exchange surface between the liquid and the abdominal cavity. Let us now pose:

$$a = \beta \frac{S_e h}{\rho_l C_l} \quad (11)$$

then the model equation is written as:

$$\frac{dT_{out}}{dt} = \frac{1}{v(t)(1-\alpha)} ((a(\alpha-1) - Q(t))T_{out} + \dots + (Q(t) - a\alpha)T_{in}(t) + a_y T_p(t) - \alpha \frac{dT_{in}(t)}{dt}) \quad (12)$$

The $\beta \in [1, 40]$ parameter is injected into the model to compensate for the assumptions of modelling such as:

- Considering the characteristics of liquid as those of water,
- A rough estimation of the heat exchange surface according to the patient's size and to the weight.

Finally, we obtain a no stationary nonlinear model with adaptable parameters.

Heat transfer model identification and optimization

Model identification and optimization will imply finding optimal values for the coefficients (α , β), i.e. such that the temperature estimated with the model (further on noted as $T_{out|M}$) fits as closely as possible to the measured one T_{out} .

In order to quantify the proximity between the measured and the estimated output temperature values, a quadratic normed criterion is used:

$$C_N = 100 \times \frac{\|\vec{T}_{out} - \vec{T}_{out|M}\|}{\|\vec{T}_{out}\|} \% \quad (13)$$

$\vec{T}_{out}$ (resp. $\vec{T}_{out|M}$) indicates a vector of measured (resp. estimated) values of $T_{out}(i)$ (resp. $T_{out|M}(i)$) at different time steps $i \in [1, \dots, N]$, separated by the sample periods dt . For example, data acquisition during 90 min with $dt = 4$ s would provide $N = 1350$ values (samples) for every measured variable.

C_N is a dimensionless value, expressed in %, independent of the number of samples (measured values) N as well as of the T_{out} signal power (amplitude). It gives a “quantified idea” of the model's precision. Model identification experience shows that models achieving a $C_N < 10\%$ can be considered as very precise; the average model's range

for C_N is usually above 10% and below 30%. Note: when $C_N > 30\%$ the estimated model adequacy is considered questionable at best.

Abdominal model identification and optimization

For model optimization purposes, T_p has been assimilated to urinary temperature T_{uri} , and input temperature has been approximated by: $T_{in} = \max(T_{in1}, T_{in2})$. Moreover the following anatomical parameters values have been chosen: $D = 10$ cm, $L = 50$ cm, $l = 50$ cm. These a priori values are result of an “average” of the observed patients’ anatomical parameters.

Two weighted coefficients have been considered in the model: $\alpha \in [0, 1]$ and $\beta \in [0, 40]$ in order to compensate the differences due to assumptions and modelling errors (exchange surface estimation, assuming that the liquid’s characteristics are those of water...).

The coefficient values were determined by trial-and-error during simulations and data according to the actual measurements, Fig. 5. A grid of C_N values has been computed, with β value steps of 5 and α value steps of 0.1. Note: that the optimal valley (talweg) looks parallel to the α -axis and that the biggest C_N variations occur along the β axis (close or over 100% in extreme cases). This clearly shows a predominant influence of the β coefficient on the model precision.

Fig. 5 Example of $C_{N\min}$ surface versus α and β . Data corresponding to an in vivo HIPEC dated July 1st, 2002

Applying the heat transfer model to clinical test data

An example of the simulation of an optimized model of Eq. (12) has been plotted on Fig. 6, corresponding to optimal values of $\alpha_{opt} = 0.7$ and $\beta_{opt} = 10$. It has been estimated on data recorded during an in vivo HIPEC which occurred on July 1st, 2002, Fig. 6.

It is notable that the discrepancies between measured and modelled temperatures are relatively small with a criterion $C_{N\min} = 8.3\%$ only. In this case the heat exchange could be modeled rather precisely.

This result is rather common for a number of HIPEC data, which confirms that the influence of the β coefficient is predominant, as can also be noted on the optimization grid, Fig. 5.

Results and discussion

Models have been validated and optimized on data from 164 in vivo IPHCs. The latter have been chosen out of more than patient’s data. Thus, only about 40% of the total available data could be thoroughly exploited a posteriori, mainly due to such problems as:

- Corrupted data acquisition files (sensor or data acquisition problems),
- Incomplete IPHCs;

Fig. 6 Model simulation results with $\alpha_{\text{opt}}=0.7$ et $\beta_{\text{opt}}=10$: $C_{N\text{min}}=8.3\%$. HIPEC of July 1st, 2002

Table 3 Numbers of occurrences of optimal values for α and β

α	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	Total
β										
0									1	1
5	2		1		2		2	6	10	23
10	24	5	5	4	1	6	8	9	16	78
15	17	3	2	2	2	2		1		29
20	4	1								5
25	1	1								2
30	3			1						4
35	1	1								2
40	2	2	3	2	3	3	1	3	1	20
Total	54	13	11	9	8	11	11	19	26	164 patients

Zone A

Zone B

- Unstable temperature produced by the heat generator (regulation problems), therefore generating input temperature instability.

The results are summed up on Table 3. It is apparent that two important model optimization zones appear; both with β -values located in the vicinity of 10, respectively gathering 48% ($\alpha \in [0,1 \text{ } 0,3]$) and 34% ($\alpha \in [0,6 \text{ } 0,9]$) of the optimized couples of values.

High values of β ($\beta \gg 1$) can be justified by the simplification hypothesis of the model, fact it indicates that the exchange surface is much bigger than what has been supposed; since it also involves e.g. the internal organs (viscera, liver...) which are supposed to be “rinsed” by the liquid.

- Zone A: 63 occurrences (38.4%) for $\alpha \in [0.1 \text{ } 0.3]$
- Zone B: 61 occurrences (37.1%) for $\alpha \in [0.6 \text{ } 0.9]$

Note in both cases the barycentre of optimal values of β is close to 10.

More detailed investigations are on their way so as to determine possible correlations between the optimal values (α_{opt} , β_{opt}) and some of the patients’ characteristics. Several other temperature probes such as oral and rectal have been used to monitor these medical procedures in US operating rooms... including them for future research. Data from MRI sensing during a heated chemotherapy test in animals for penetration figures etc.

Conclusion

One of the main difficulties that the surgeon has to cope with during closed-abdomen IPHC is how to maintain a uniform temperature of the liquid close to the desired value (about 42 °C) throughout the treatment. For example, a brief analysis of several temperature curves measured in vivo during IPHC has shown that the “Mesentery” temperature was usually unstable and in most cases it did not reach the targeted

42 °C. A better understanding of the heat transfer within the abdomen could lead to a more optimal temperature dispatch. The development of a specific optimization tool as outlined in this paper, will help in the in vivo IPHC optimization task.

Future investigations should be concerned with the determination and identification of possible correlations between the estimated optimal coefficients (α_{opt} , β_{opt}) and some of the patients' characteristics. Indeed, we can use the patient's height, weight, corporal surface. Also the type and extent of the previous surgical intervention(s), as well as the intermediary temperatures modeling (e.g. mesentery). In order to be statistically relevant, research must treat data of larger number of patients.

Thus a validated IPHC model, being able to estimate various temperature values in real-time (or: anticipate events before they occur) will help to establish a reliable, real-time (on-line) supervision and optimization methodology for in vivo IPHC. This developed model must be based on thermal knowledge as well as on anatomical characteristics of the patients. It can therefore be qualified as a knowledge model rather than a behaviour model, which offers a wide scope of possible future adaptations to the particular patient characteristics.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest regarding the publication of this paper.

References

- Barkin N, Classe JM, Pomel C, Gouy S, Chene G, Glehen O (2014) Hyperthermic intraperitoneal chemotherapy (HIPEC) in ovarian cancer. *J Visc Surg*. <https://doi.org/10.1016/j.jvisc Surg>
- Bird RB, Stewart WE, Llightfoot EN (2006) Transport phenomena, 2nd edn. Wiley, New York
- Clitan I, Loga D, Muresan V, Stora N, Sita V, Lungoci C, Mironiuc A (2015) Design of a Temperature Controller for an Hyperthermic Intraperitoneal Chemotherapy Equipement. In: 10th Jubilee IEEE International Symposium on Applied Computational intelligence and Informatics, Timisoara, Romania ISBN 978-1-4799-9911-8/15
- Detroz B, Elias D, Damia E, Debaene B, Rougier P, Lasser P (1994) La chimio-hyperthermie (CHIP), un traitement prometteur mais encore mal connu de la carcinose péritonéale. *Bull Cancer* 81:182–193
- Dubé P, Lasser PH, Elias D (1997) Traitement de carcinose péritonéale d'origine colorectale. *J Chir* 134(5):233–236
- EFS <http://www.efs.fr/english/medical/medical.htm>. Accessed 26 June 2017
- Fujimoto S, Takahaschi M, Motou T, Kobayashi K, Toyosawa T, Isaxa E, Sumida M, Ohkubo H (1997) Improved mortality rate of gastric carcinoma patients with peritoneal carcinomatosis treated with intraperitoneal hyperthermic chemoperfusion combined with surgery. *Cancer* 79(5):884–891
- Gilly FN, Carry PY, Sayag AC, Brachet A, Panteix G, Salle B, Bienvénu J, Burgard G, Guibert B, Bansillon V, Braillon G (1994) Regional chemotherapy (with mitomycin C) and intra-operative hyperthermia for digestive cancers with peritoneal carcinomatosis. *Hepatogastroenterology* 41:124–129
- Glehen O, Sayag-Baujard AC, Gilly FN (2004) Peritoneal carcinomatosis treated with surgery and intraperitoneal chemohyperthermia: 14 years experience in Lyon. *The Internet Journal of Medical Technology*, 1(2). <http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijmt/vol1n2/chemohyper.xml>. Accessed 12 June 2017
- Goldstein P, Gomes Da Silva R, Cabanas J, Sugarbaker PH (2005) Management of peritoneal carcinomatosis from colon cancer, gastric cancer and appendix malignancy. *Cancer Ther* 3:299–320
- Gomez-Portilla A, Inaki Cendoya I, Lopez De Tejad I, Olbarri I, Magarch L, Martinez De Lecea C, Gil A, Valdovinos M, Larabide I, Ruiz De Alegria N, Fernandez JL, Cachorro I, Del Carmen Contreras M, Castaneda J, Uriarte A, Boado MV, Uteri JA, Ulibarrena MA (2005) Bases y fundamentos del tratamiento de la carcinomatosis peritoneal por cáncer colorectal. *Cir Esp* 77(1):6–17
- Hilderbrandt B, Wust Ahlers O (2002) The cellular and molecular basis of hyperthermia. *Crit Rev Oncol* 43:33–56
- Jähne J, Piso P, Schmoll E, Haulitschek-Haus R, Sterzenbach H, Paul H, Pichlmayer R (1997) Intraoperative (hyperthermie) intraperitoneale chemotherapie—Überlegungen und Aspekte zum sicheren intra-und postoperativen Umgang mit Zytostatika. Springer, Berlin/Heidelberg, pp 1435–2443
- Ladhari T, Szafnicki K, Cournil M, Pinoli JC (2005) Modelling and simulation of some aspects of the in vivo abdominal cancer treatment. SMC 2005. 11th International Conference System Modelling Control, Zakopane, Poland vol. 2, pp. 17–21
- Lungoci C, Moga D, Muresan V, Petreus D, Stora N, Moga R, Munteanu M, Raus J, Munteanu V, Mironiuc A (2015a) hyperthermic intraperitoneal chemotherapy approach based on cyber-physical system paradigm. *CEAI* 17(3):50–59
- Lungoci C, Muresan V, Moga D, Clitan I, Moga R, Sita V, Oniu T, Mironiuc A (2015b) Advanced temperature control for innovative HIPEC equipment. *Proced Comput Sci* 64:497–505
- Pang L, Shen L, Zhong Z (2016) Mathematical modelling and analysis of the tumor treatment regimens with pulsed immunotherapy and hemotherapy. *Comput Math Methods Med*. <https://doi.org/10.1155/2016/6260474>
- Porcheron J, Talabard JN, Breton C, Szafnicki K, Luxembourger O, Dufraisse G, Mille D, Clavreul G, Mosnier JF, Perpoint B (2000) Intraperitoneal chemohyperthermia for peritoneal carcinomatosis: original modelling, clinical tolerance and results study about 30 patients. *Hepatogastroenterology* 47(35):1411–1418
- Salle B, Gilly FN, Carry PY, Sayag AC, Brachet A, Braillon G (1993) Chimio-hyperthermie intrapéritonéale dans le traitement des carcinoses péritonéales d'origine ovarienne. *Obstel Biol* 22:269–371
- Simbawa E (2017) Mechanistic model for cancer growth and response to chemotherapy. *Comput Math Methods Med*. <https://doi.org/10.1155/2017/3676295>
- Sugarbaker PH (1995) Peritonectomy procedures. *Ann Surg* 221:29–42
- Sugarbaker PH, Jablonsky JA (1995) Prognostic features of 51 colorectal and 130 appendiceal cancer patients with peritoneal carcinomatosis treated by cytoreductive surgery and intraperitoneal chemotherapy. *Ann Surg* 221:124–132

- Szafnicki K, Cournil M, O'meara D, Talabard JN, Porcheron J, Schmit T, Balique JG (1998) Modélisation de la chimiohyperthermie intrapéritonéale: étude expérimentale et identification de certains aspects thermiques. *Bull Cancer* 85(2):160–166
- Szafnicki K, Cournil K, O'meara D, Talabard JN, Porcheron J (2000) Modelling and supervision of intraperitoneal chemohyperthermia (IPCH). *Proceedings of the 4th IFAC Symposium on Modelling and Control in Biomedical Systems—BIOMED*, Karlsburg/Greifswald, Germany, pp. 187–190, ISBN: 0-08-043549-1
- Vander Zee J (2002) Heating the patient: a promising approach. *Ann Oncol* 13:1173–1184
- Welty JR, Wichx CE, Wilson RE, Rorrer G (2001) *Fundamentals of momentum, heat, and mass transfer*, 4th edn. Wiley, New York, p 782
- Yonemura Y, Fujimura T, Fushida S, Takegawa S, Kamata T, Katayama K, Kosaka T, Yamagichi A, Miwak K, Miyazaki I (1991) Hyperthermo-chemotherapy combined with cytoreductive surgery for the treatment of gastric cancer with peritoneal dissemination. *World J Surg* 15:530–536