The Theory of Semipermeable Vesicles and Membranes —an Integral-Equation Approach III. Vesicles with Internal Non-permeating Ions

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January 11, 1989

ABSTRACT

The system of a fluid in the presence of a spherical semipermeable vesicle (SPV) with the freely mobile non-permeating species *inside* the vesicle is investigated via an integral-equation approach. This system can be used to model certain feature of a bilogical cell, permeable to simple ions, in which solute proteins inside the cell are unable to permeate its walls. As an illustrative example of the use of our integral equations, the analytical solution for denisty profiles in the Mean-Spherical-Approximation/Debye-Hückel approximation is obtained. Here, the notation A/B denotes the use of approximation A to obtain the density profiles near a membrane and approximation B to obtain the bulk pair correlation functions. A method which may apply to the system of proteins fixed inside a cell is suggested.

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I. INTRODUCTION

In our previous papers[1,2], we obtained general integral equations for a fluid in the presence of a plane semipermeable membrane (SPM) or a spherical semipermeable vesicle (SPV), where the non-permeating species (NPS) are restricted to one side of the plane membrane or outside the spherical vesicle. Analytic results were obtained for the permeating-species density ratios between the two sides of a plane SPM as well as the density profiles of charged hard spheres near a charged SPM or SPV in the mean-spherical approximation/Debye-Hückel approximation (MSA/DH). Here and below, the notation A/B denotes the use of approximation A to obtain the density profiles near a membrane and approximation B to obtain the bulk pair correlation functions.

The purpose of this paper is to investigate a fluid in the presence of a spherical SPV with the NPS *inside* the vesicle and freely mobile. We shall study two types of distributions of NPS inside a vesicle. In one, the NPS freely mobile inside the vesicle, while in the other the NPS fixed inside the vesicle. These two types of systems are both relevant to the modelling of a biological cell.

Our model for a system of a solute ions near and inside a spherical SPV with the NPS *inside* the vesicle is very similar to the model we used earlier for the system with the NPS *outside* the vesicle. The main difference is that the SPV acts as a pore to the NPS in the former case, while it acts as a hard-core to the NPS in the latter case. Fluids inside a slit[3], spherical[3], and cylindrical[4] pores have also been investigated by us via an integral-equation approach[3-4]. These pore systems can be equivalently regarded as SPMs and SPVs with the NPS inside the vesicle, with the permeating species (PS) regarded as fully permeable continuum solvents, as we have mentioned earlier.[1] The work here and in refs 1 and 2 can be reviewed as extensions of those systems, in which some of the solute species as well as the solvent are permeating species. The integral equation method we have used in treating pore systems[3-4] are combined here with the method we

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have already used in treating membrane systems[1-2] to apply to a system of a permeable solute particles in the presence of a a spherical SPV with the NPS inside the vesicle.

In section II of this paper, general integral equations are given for both protein fixed and unfixed systems. an analytical solution for ionic fluids in the MSA/DH approximation is obtained in section III. The numerical results are discussed in section IV.

II. GENERAL FORMULATION

A. Freely Mobile Non-permeable Species inside a Vesicle

In our previous papers[1,2], we obtained from an Ornstein-Zernike (OZ) approach, for the spherical SPV system, the equations

$$
\begin{aligned}
h_{im}(r) &= c_{im}(r) + \sum_{l \neq m} \rho_l h_{il} * c_{lm} \\
&= c_{im}(r) + \sum_{l \neq m} \rho_l h_{ml} * c_{li}
\end{aligned}
\tag{2.1a}
$$

or

$$
h_{im}(r) - c_{im}^S(r) = (h * c^S)_{mi}(r) - \lambda z_i I_m(r) \tag{2.1b}
$$

$$
\nabla^2 I_m(r) = -4\pi \sum_l z_l \rho_l h_{lm}(r) \tag{2.2}
$$

with boundary conditions

$$
\frac{dI_m(r)}{dr}\Big|_{r-R_m \to 0^+} - \frac{dI_m(r)}{dr}\Big|_{r-R_m \to 0^-} = -\frac{z_m}{R_m^2} \tag{2.3a}
$$

$$
\frac{dI_m(r)}{dr}\Big|_{r \to 0} = 0 \tag{2.3b}
$$

$$
\frac{dI_m(r)}{dr}\Big|_{r \to \infty} = 0 \tag{2.3c}
$$

$$
I_m(0) = 4\pi \sum_l \rho_l z_l \int_0^\infty s\, ds\, h_{lm}(s) \tag{2.3d}
$$

where

$$
c_{ij}^L \equiv -\beta u_{ij}^E(r) = -\lambda z_i z_j / r \tag{2.4}
$$

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$$c_{ij}^S \equiv c_{ij} - c_{ij}^L \tag{2.5}$$

$$\lambda z_j I_i(r) \equiv -[c_{ij}^L + (h * c^L)_{ij}] \tag{2.6}$$

$$\lambda \equiv \frac{e_{el}^2}{\epsilon k_B T} \equiv \frac{\Lambda}{4\pi} \tag{2.7}$$

Here, the subscript m denotes the membrane properties while subscripts i, j, and l denote the ionic species. The h and c are the pair correlation function and direct pair correlation function respectively, z_i and ρ_i are the charge number and bulk number density[5] of ionic species i respectively, e_{el} is the electronic charge, $\beta = 1/k_B T$, k_B is Boltzmann's constant, T is temperature, ϵ is the dielectric constant of the continuum solvent, Γ is Debye length, while z_m and R_m are the charge number and radius of the vesicle respectively. I_m is the electric potential distribution of the membrane. If $z_i \equiv 0$, we recover the equations for a non-ionic solution near a SPV.

We need another equation to supplement the OZ equation in order to have a closed system of equations. If one uses the mean spherical approximation (MSA),[6] then, denoting the ion-membrane short-range interaction potential as $u_{im}^S(r)$, we have

$$c_{im}^S(r) = -\beta u_{im}^S(r) \equiv -\beta[u_{im}(r) - u_{im}^E(r)] \quad \text{if } u_{im}^S(r) < \infty \tag{2.8a}$$

$$h_{im}(r) = -1 \quad \text{if } u_{im}^S(r) = \infty \tag{2.8b}$$

If one uses the hypernetted-chain (HNC) closure, then, one has[6]

$$h_{im}(r) - c_{im}^S(r) = \ln(1 + h_{im}(r)) + \beta u_{im}^S(r) \tag{2.9}$$

More complicated closures are discussed in I, including an exact closure and approximate non-local density-functional closures. We hope to investigate such approximate closures in further work; the closures we consider here have been chosen to provide reasonable benchmarks against which to compare future results.

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In the simplest case, if we consider an ideal spherical SPV, which is fully permeable to some ionic species, but acts as a charged hard spherical pore for the non-permeating ions, we have

$$u_{im}^S(r) = \begin{cases} 0 & r < (d_m - d_i)/2 \\ \infty & r > (d_m - d_i)/2 \end{cases} \qquad (2.10a)$$

when the ion is impermeable to the membrane, and

$$u_{im}^S(r) = 0 \qquad (2.10b)$$

otherwise. Here, d_i is the diameter of ion species i and $d_m = 2R_m$ is the diameter of the membrane.

We begin with a known bulk density[5] ρ_i of particle species i and obtain the bulk correlation functions via various approximations. Then, substituting the bulk correlation functions into eq.(2.1), we can solve eq.(2.1a) with closures (2.8), (2.9), or some other closure[1] to obtain the density profiles,

$$\rho_i(r) = \rho_i[1 + h_{im}(r)] \quad , \qquad (2.11)$$

charge profiles,

$$q(r) = \sum_l z_l e_{el} \rho_l h_{lm}(r) \quad , \qquad (2.12a)$$

and the electric-potential profile $I_m(r)$ from eq. (2.1b). The average density inside a vesicle can be easily obtained when $\rho_i(r)$ is known:

$$\bar{\rho}_i = \rho_i[1 + \frac{3}{R_m^3} \int_0^{R_m} r^2 h_{im}(r) dr] \qquad (2.12b)$$

When $r \to \infty$, we have [cf. eq.(2.1)],

$$h_{im}(\infty) = c_{im}(\infty) + \sum_l \rho_l \bar{h}_{il}(0) c_{lm}(\infty) \qquad (2.13a)$$

$$h_{im}(+\infty) - c_{im}^S(+\infty) = \sum_l \rho_l \bar{c}_{il}^S(0) h_{lm}(+\infty) - \lambda z_i I_m(+\infty) \qquad (2.13b)$$

where the tilde denotes the three-dimensional Fourier transformation,

$$\tilde{f}(k) = 4\pi \int_0^\infty r \frac{\sin(kr)}{k} f(r) \quad .$$

(2.14)

It turns out that eqs.(2.13) and (2.14) are exactly the same as eqs. (3.1) and (3.8) of ref. 2 in the plane membrane problem. As we have mentioned earlier[2], this is because bulk density ratios and membrane potentials are only dependent on the electrochemical potentials of bulk solutions, which are unaffected by the detailed properties of a SPM.

Therefore, we also have, for a simple three-component system with permeating cation(+), anion(-) and nonpermeating protein (p), in the MSA,

$$c_{pm}(+\infty) = \frac{-1}{1 + \rho_p \tilde{h}_{pp}(0)}, \quad c_{im}(+\infty) = 0$$

(2.15)

$$h_{im}(+\infty) = \frac{\rho_i'}{\rho_i} - 1 = \frac{-\rho_p \tilde{h}_{ip}(0)}{1 + \rho_p \tilde{h}_{pp}(0)}$$

(2.16)

$$\lambda z_i I_m(+\infty) = \sum_l \rho_l \tilde{c}_{il}^S(0) h_{lm}(+\infty) - h_{im}(+\infty)$$

(2.17)

where the ion species i is a cation or anion and $\rho_i' \equiv \rho(+\infty)$. For the HNC approximation, we have a set of nonlinear equations [eqs. (2.13) and (2.14) with (2.9)] that can be easily solved by standard numerical methods.[2]

B. Nonpermeable Species Fixed inside a Vesicle

When the NPS are fixed inside a membrane instead of being mobile, the NPS can be taken to be a part of membrane. As a result, the total PS-membrane pair potential can be obtained from

$$\bar{u}_{im}(r) = u_{im}(r) + \sum_p \int u_{ip}(|\mathbf{r} - \mathbf{r}_p|)\rho_p(r_p)d\mathbf{r}_p$$

(2.18)

where the subscript p is the species label of the NPS and $\rho_p(r)$ is the fixed density distribution of the NPS inside a vesicle. (We have assumed that the distribution is

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orientational independent). Once $\bar{u}_{im}(r)$ is known, we can solve integral equations (2.1a) and (2.8-9) which contain the PS only. Here, the density for ions ρ_i is the bulk density of ions far away from the vesicle.

For example, when there is one NPS (the only one) situated on the shell $r = L$ inside the vesicle and concentres to its walls, we have,

$$\rho_p(r) = \frac{\delta(r-L)}{4\pi L^2} \tag{2.19}$$

Substituting eq. (2.12) into (2.11) and taking the $L \to 0$ limit, we obtain

$$\bar{u}_{im}(r) = u_{im}(r) + u_{ip}(r), \quad L \to 0 \tag{2.20}$$

If the vesicle is ideal ($u_{im}(r) = 0$), we have system of one fixed ion immersed in the solution, which consists of the permeable species only. This is what we expected.

III. THE ANALYTICAL SOLUTION IN THE MSA/DH APPROXIMATION

For simplicity, we only consider a three-component system: cation (+), anion (-), and a NPS — protein or polymer ion — (p) which is freely mobile inside a vesicle. If we use the DH approximation for the bulk correlations, we have[6]

$$c_{ij}^S(r) = 0 \tag{3.1}$$

which leads to [cf. (2.1b), (2.8), (2.10), (2.2)]

$$\frac{1}{r}\frac{d^2(rI_m)}{dr^2} = \begin{cases} 4\pi\lambda(z_+^2\rho_+ + z_-^2\rho_- + z_p^2\rho_p)I_m(r) & r < (d_m - d_p)/2 \\ 4\pi\lambda(z_+^2\rho_+ + z_-^2\rho_-)I_m(r) + 4\pi z_p\rho_p & r > (d_m - d_p)/2 \end{cases} \tag{3.2}$$

Solving with the boundary condition (2.3), we have,

$$I_m(r) = \begin{cases} A_1 e^{\kappa r}/r - A_1 e^{-\kappa r}/r & 0 < r < s_{mp} \\ B_1 e^{\alpha r}/r + B_2 e^{-\alpha r}/r + I_m(+\infty) & s_{mp} < r < R_m \\ A_2 e^{-\alpha r}/r + I_m(+\infty) & R_m < r < \infty \end{cases} \tag{3.3}$$

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with

$$\kappa \equiv \sqrt{4\pi\lambda\sum_l \rho_l z_l^2} \qquad (3.4)$$

$$\alpha \equiv \sqrt{4\pi\lambda(\rho_+ z_+^2 + \rho_- z_-^2)} \qquad (3.5)$$

$$\lambda I_m(+\infty) = \frac{-z_p\rho_p}{\rho_+ z_+^2 + \rho_- z_-^2} \qquad (3.6)$$

$$B_1 = \frac{z_m}{2R_m\alpha}e^{-\alpha R_m} \qquad (3.7)$$

$$A_1 = \frac{z_m\exp[-\alpha d_p/2] + (1 + \alpha s_{mp})R_m I_m(+\infty)}{[(\kappa+\alpha)\exp(\kappa s_{mp}) + (\kappa-\alpha)\exp(-\kappa s_{mp})]R_m} \qquad (3.8)$$

$$B_2 = A_1 e^{(\kappa+\alpha)s_{mp}} - A_1 e^{(\alpha-\kappa)s_{mp}} + s_{mp}I_m(+\infty)e^{\alpha s_{mp}} - B_1 e^{2\alpha s_{mp}} \qquad (3.9)$$

$$A_2 = B_2 + \frac{z_m}{2\alpha R_m}e^{\alpha R_m} \qquad (3.10)$$

Then we have the density profiles from eqs.(2.1b),(2.11)

$$h_{\pm m}(r) = -\lambda z_\pm I_m(r) \qquad (3.11a)$$

$$h_{pm}(r) = -\lambda z_p I_m(r) \quad r > s_{mp}$$
$$= -1 \quad r < s_{mp} \qquad (3.11b)$$

The average density inside the vesicle can be obtained from eq.(2.12).

Fig.1. shows that the average densities of ions inside a vesicle as a function of the average density of protein in the cases of both charged and uncharged membrane when bulk density $\rho_+(+\infty)$ is fixed. The density profiles, electric potential profile, and charged profiles are also shown in Figs.2-5.
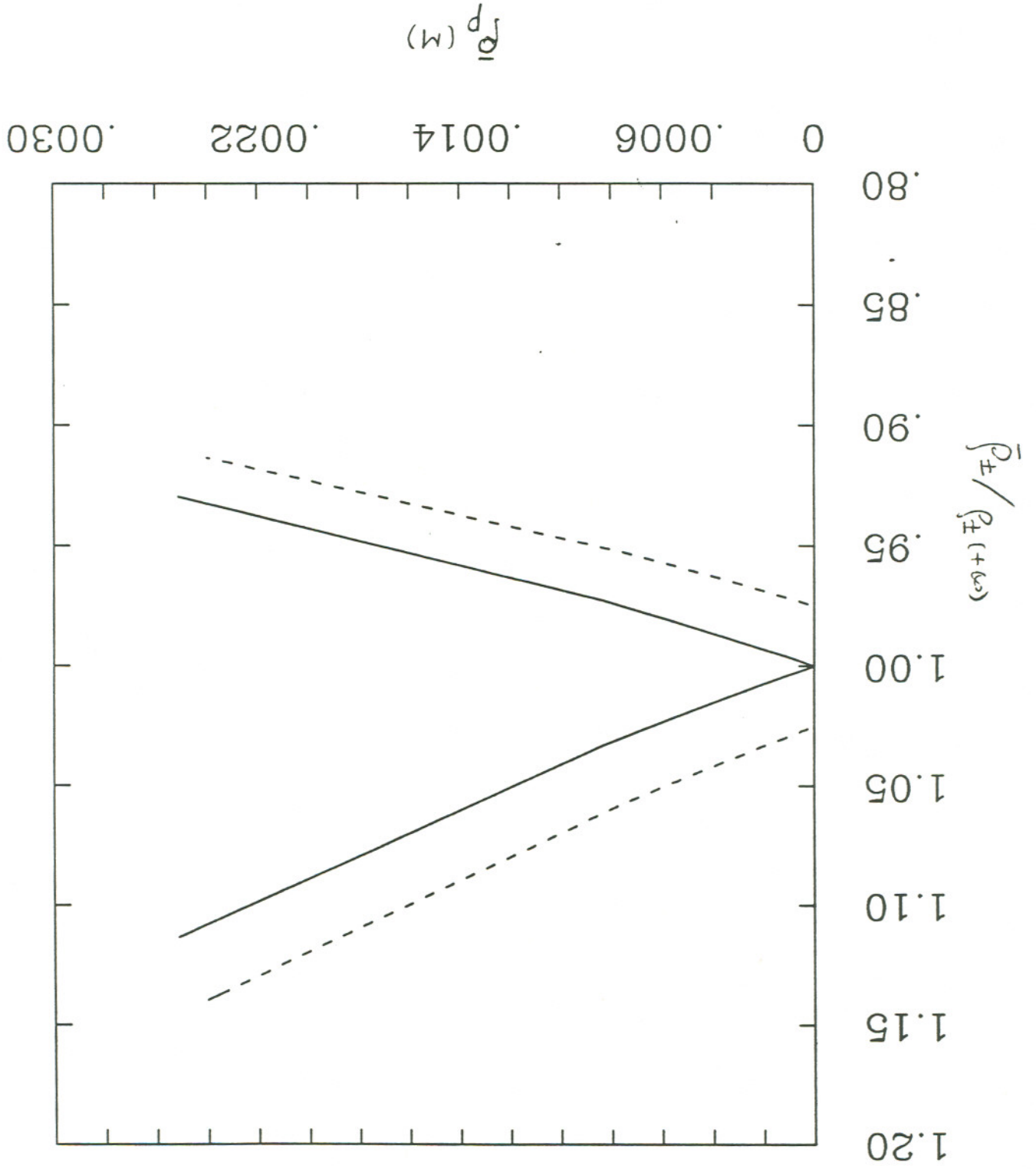
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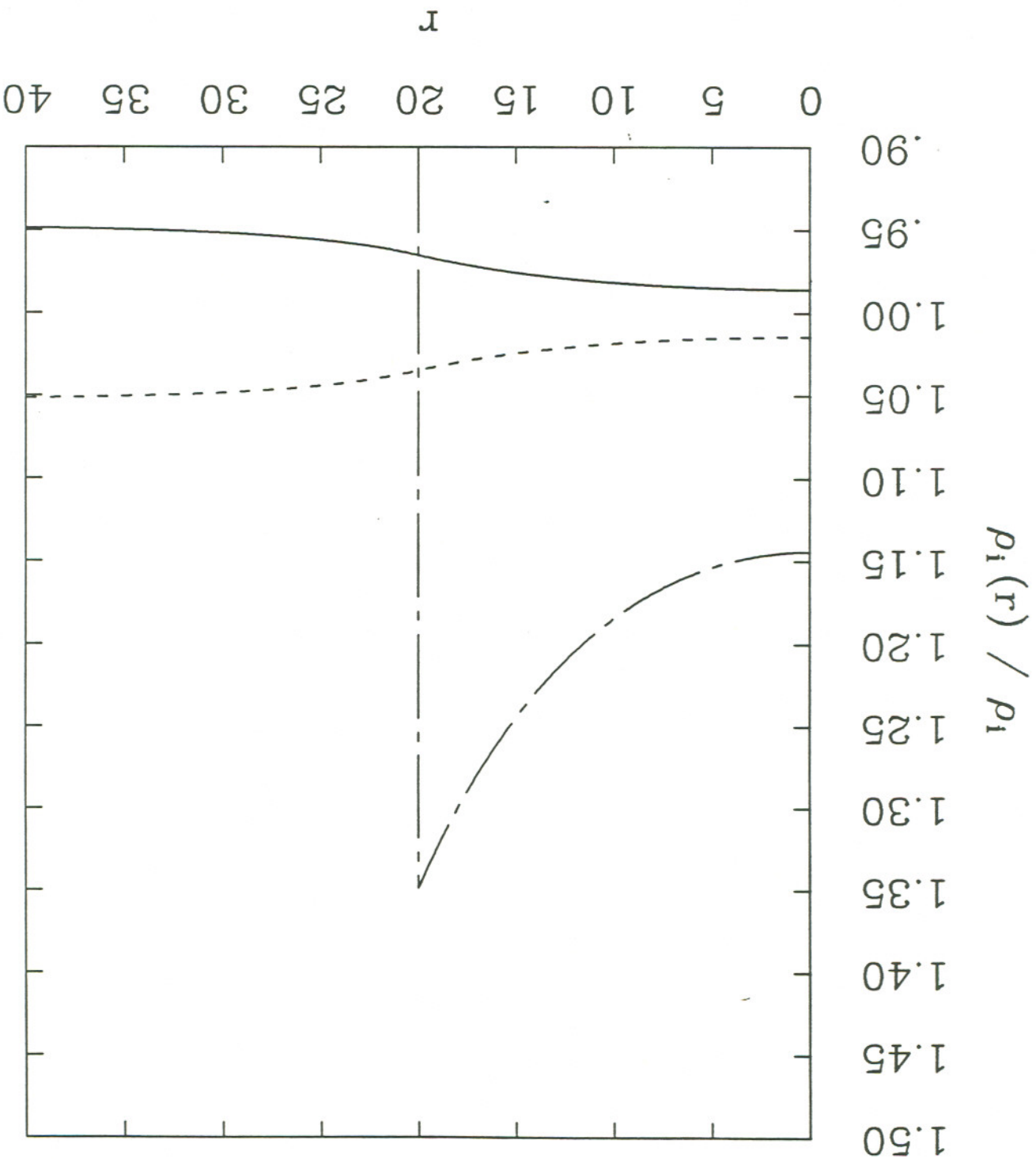[3]. Y. Zhou and G. Stell, SUSB CEAS report#502 (Feb. 1988) ; *Mol. Phys.* (to appear).

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FIGURE CAPTIONS

Fig.1. The average densities of cations and anions, $\bar{\rho}_{\pm}$, inside a SPV [reduced by the $\rho_{\pm}(+\infty)$] as a function of average density of the NPS $\bar{\rho}_p$ (M). Here $\rho_{\pm}(+\infty) = 0.1M$, $z_{\pm} = \pm 1$, $z_p = -10$, $d_p = 20$Å, $d_m = 60$Å, $T = 298.16K$, $\epsilon = 78.54$. The upper pair of lines are the results for cations and lower pair of lines are for the anions. $z_m = 0$ (—), $z_m = -1$ (- - -).

Fig.2. The density distributions for cation (—), anion (- - -), and protein-like ions (— - —) as a function of the distance from the center of the SPV, r (Å), in the MSA/DH approximation. $\rho_+ = 0.1M$, $\rho_p = 0.001M$, $z_m = 0$. Other parameters as in Fig.1.

Fig.3. The charge profile, $q(r)/e_{el}$ (M), (—) and potential profiles, $\lambda I_m(r)$, (- - -) as a function of the distance, r (Å). Parameters as in Fig.2.

Fig.4. The density distributions for cation (—), anion (- - -), and protein-like ions (— - —) as a function of the distance from the center of the SPV, r (Å), in the MSA/DH approximation. Parameters as in Fig.2 except $z_m = -1$.

Fig.5. The charge profile, $q(r)/e_{el}$ (M), (—) and potential profiles, $\lambda I_m(r)$, (- - -) as a function of the distance, r (Å). Parameters as in Fig.4.
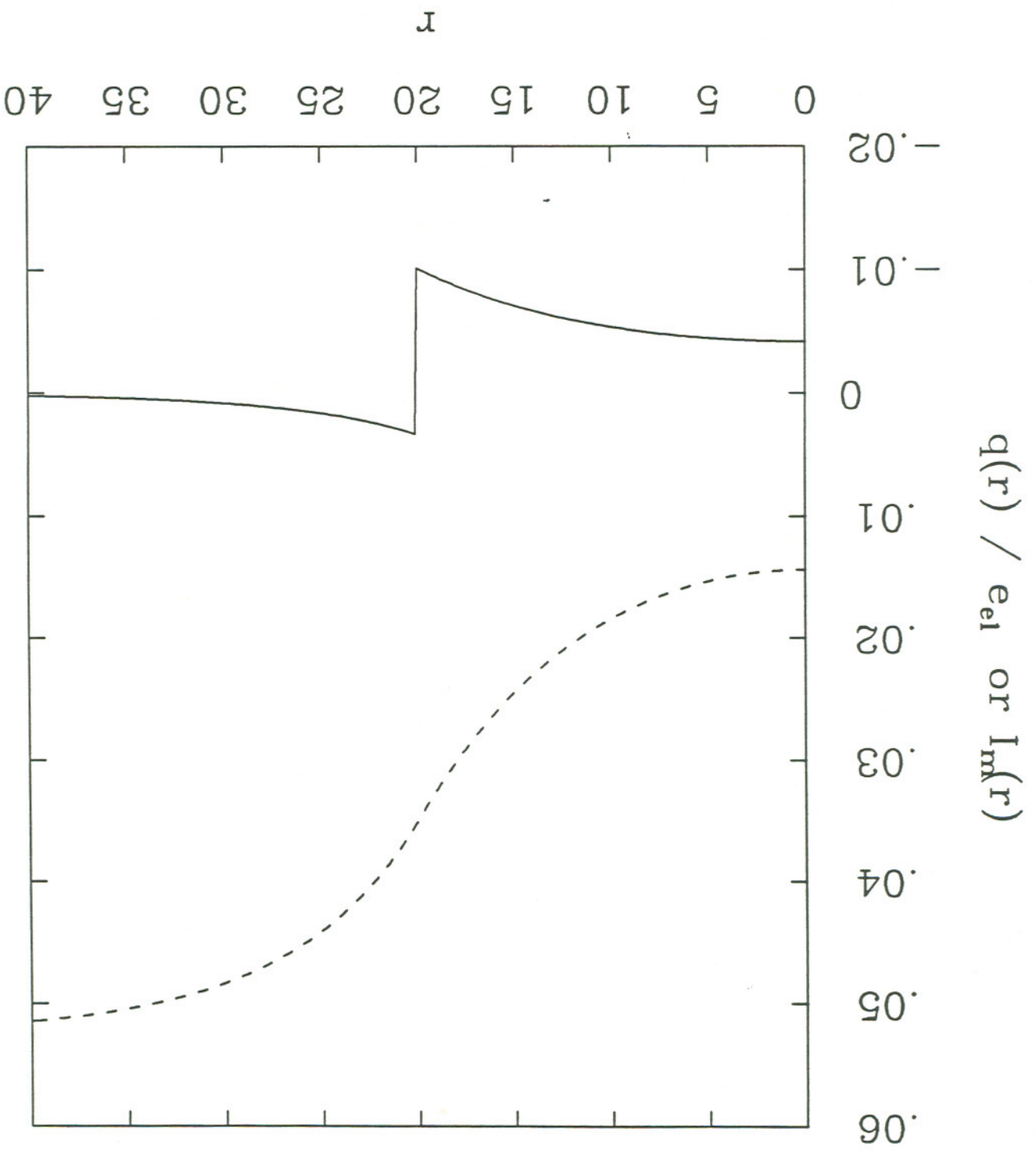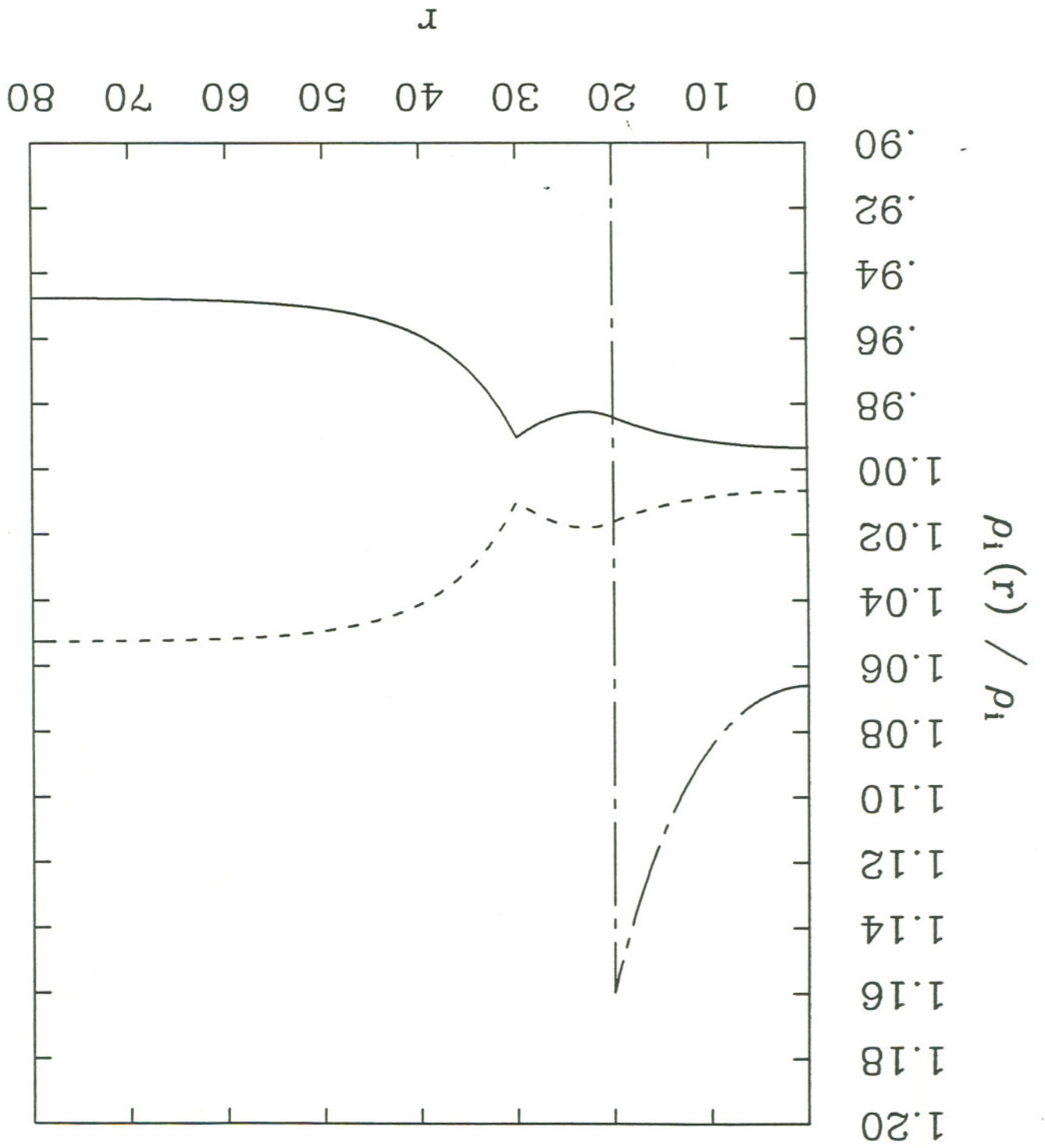
Fig. 1

$\bar{\rho}_p$ (M)

.0030 .0022 .0014 .0006 0

.80 .85 .90 .95 1.00 1.05 1.10 1.15 1.20

$\bar{\rho}_+ / \bar{\rho}_+(\varepsilon+s)$

Fig. 2

Fig. 3

Fig. 4

r

0   10   20   30   40   50   60   70   80

$\rho_i(r) / \rho_i$

.90 .92 .94 .96 .98 1.00 1.02 1.04 1.06 1.08 1.10 1.12 1.14 1.16 1.18 1.20

Fig. 5

r

$q(r) / e_{el}$ or $\lambda I_m(r)$

0 10 20 30 40 50 60 70 80

$-.01$ 0 .01 .02 .03 .04 .05 .06