$O(\mathrm{N}^2)$ ALGORITHM FOR COMPUTING VOLUME OF OVERLAPPING SPHERES

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ABSTRACT

An exact analytical method for the calculation of volume of overlapping spheres is presented. In the considered procedure volume of overlapping spheres is expressed as surface integrals over closed regions. Using a natural continuous correspondence between the points of the sphere surface and the points of the plane the surface integrals are computed by the next transformation onto double integrals which are reduced onto curve integrals.

Keywords: *parametrization, volume of overlapping spheres*

1. INTRODUCTION

Richmond [13] has defined the solvent-excluded volume to mean the volume contained within the solvent accessible surface, i.e. the volume which is inaccessible to the centres of solvent particles. That is the union of the expanded atom spheres. The excluded volume is an important quantity in the theory of gases and liquids [9]. The exploration of molecular volume and surface is essential for the understanding of drug action since short range dispersion forces play a major role in the binding of drug molecules to receptors.

The problem of the computation of volume of the union of overlapping spheres has been the subject of methods both numerical [5, 11, 14] and analytic [6–8, 12, 13].

2. PARAMETRIZATION OF THE SPHERE

In this paper we are concerning with calculation of volume of overlapping spheres. We assume that a molecule S consisting of atoms $S_1, \cdots, S_n$. Hence $S = \bigcup\limits_{j=1}^{n} S_j$. Let (x_i, y_i, z_i) be Cartesian coordinates of the centre of the i-th sphere and r_i be the radius of this sphere, where $1 \leq i \leq n$. Then the points (x, y, z) of the the i-th sphere satisfy

$$(x - x_i)^2 + (y - y_i)^2 + (z - z_i)^2 \leq r_i^2 \qquad (1)$$

and for the points the i-th sphere surface the equation

$$(x - x_i)^2 + (y - y_i)^2 + (z - z_i)^2 = r_i^2 \qquad (2)$$

holds. The equations

$$
\begin{aligned}
x &= x_i + \frac{4r_i^2 t}{t^2 + s^2 + 4r_i^2} \\
y &= y_i + \frac{4r_i^2 s}{t^2 + s^2 + 4r_i^2} \\
z &= z_i + r_i - \frac{8r_i^3}{t^2 + s^2 + 4r_i^2}
\end{aligned}
\qquad (3)
$$

describe a relation between the points of the tangent plane $(t, s) \in R^2$ and the points of the sphere surface, except the point $(x_i, y_i, z_i + r_i)$ called *North Pole*. The equations

$$
\begin{aligned}
t &= -2r_i \frac{x - x_i}{z - z_i - r_i} \\
s &= -2r_i \frac{y - y_i}{z - z_i - r_i}
\end{aligned}
\qquad (4)
$$

express the inverse transformation. Equations (3) and (4) represent a projection of the points of the i-th sphere surface onto the (t, s) plane with respect to its *North Pole* . The points of the i-th sphere which are outside of the j-th sphere, satisfy (1) and the following inequality

$$(x - x_j)^2 + (y - y_j)^2 + (z - z_j)^2 \geq r_j^2. \qquad (5)$$

On the other hand, the points of the i-th sphere surface which are outside of the j-th sphere, satisfy (2) and (5). Transformation of those points into (t, s) plane leads to

$$a_j^i(t^2 + s^2) + b_j^i t + c_j^i s + d_j^i \geq 0, \qquad (6)$$

where

$$
\begin{aligned}
a_j^i &= (x_i - x_j)^2 + (y_i - y_j)^2 + (z_i + r_i - z_j)^2 - r_j^2 \\
b_j^i &= 8r_i^2(x_i - x_j) \\
c_j^i &= 8r_i^2(y_i - y_j) \\
d_j^i &= 4r_i^2 \left[(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - r_i - z_j)^2 - r_j^2 \right].
\end{aligned}
\qquad (7)
$$

For $j \neq i$ we say that S_j is a neighbor of S_i if $S_i \cap S_j \neq \emptyset$. We shall compute volume $V(S)$ by using Gauss-Ostrogradsky theorem which allows to reduce volume $V(S)$ to the surface integrals

$$V(S) = \iiint\limits_{S} dx\,dy\,dz = \iint\limits_{H(S)} z\,dx\,dy = \sum_{i=1}^{n} \iint\limits_{H_i(S)} z\,dx\,dy, \qquad (8)$$

where $H(S)$ is the surface of S and $H_i(S)$ is as a part of surface of S_i which is outside of all its neighbors. Let us denote by Ω_i the set of points of (t, s) plane which correspond $H_i(S)$. Define $\Psi_i = \{j; S_j$ is a neighbor of $S_i\}$. So Ψ_i is a set of indexes of neighbors of S_i. Then

$$\Omega_i = \{(t, s); \ a_j^i(t^2 + s^2) + b_j^i t + c_j^i s + d_j^i \geq 0 \ \text{for all} \ j \in \Psi_i\}. \qquad (9)$$

Since (6) represents either interior of a circle ($a_j^i < 0$) or exterior of a circle ($a_j^i > 0$) or half plane ($a_j^i = 0$) then Ω_i is an intersection of those parts of (t, s) plane . It is easy to

see that if S_i has no neighbors then $\Omega_i = R^2$ and $H_i(S)$ is all surface of S_i and the corresponding surface integral is equal $(4/3)\pi r_i^3$. On the other hand, if *surface of* $S_i \subset \bigcup\limits_{j\in\Psi_i} S_j$ then $\Omega_i = \emptyset$ and $H_i(S) = \emptyset$.

The problem of computing $V(S)$ is now reduced to computing of n surface integrals.

3. COMPUTATION OF $\iint\limits_{H_I(S)} Z DX DY$

For the computing of surface integrals in (8) we will use the known formula which transforms the surface integral into double integral. Denote

$$
J_i(t,s) = \begin{vmatrix} \dfrac{\partial x}{\partial t} & \dfrac{\partial x}{\partial s} \\[2mm] \dfrac{\partial y}{\partial t} & \dfrac{\partial y}{\partial s} \end{vmatrix}
$$

then in view of (3) we have

$$
J_i(t,s) = 16 r_i^4 \frac{4r_i^2 - t^2 - s^2}{(t^2 + s^2 + 4r_i^2)^3}.
$$

Consequently,

$$
\iint\limits_{H_i(S)} z\,dxdy = -\iint\limits_{\Omega_i} \left(z_i + r_i - \frac{8r_i^3}{t^2 + s^2 + 4r_i^2} \right) J_i(t,s)\,dtds
$$

$$
= 128 r_i^7 \iint\limits_{\Omega_i} \left(\frac{\partial Q(t,s)}{\partial t} - \frac{\partial P(t,s)}{\partial s} \right) dtds
$$

(10)

where

$$
Q(t,s) = \frac{1}{3} \frac{t}{(t^2 + s^2 + 4r_i^2)^3} +
$$

$$
\frac{t}{(t^2 + s^2 + 4r_i^2)^2} \left(\frac{1}{48r_i^2} - \frac{z_i + r_i}{2} \right) + \frac{1}{192r_i^4} \frac{t}{(t^2 + s^2 + 4r_i^2)},
$$

$$
P(t,s) = \frac{1}{3} \frac{-s}{(t^2 + s^2 + 4r_i^2)^3} +
$$

$$
\frac{-s}{(t^2 + s^2 + 4r_i^2)^2} \left(\frac{1}{48r_i^2} - \frac{z_i + r_i}{2} \right) + \frac{1}{192r_i^4} \frac{-s}{(t^2 + s^2 + 4r_i^2)}.
$$

It is useful to observe that if $\Omega_i = R^2$ then the integrals in (10) are equal $(4/3)\pi r_i^3$.

At first, we assume that Ω_i is bounded. Then applying Green's theorem to (10) we transform double integral into the following curve integrals. Hence,

$$
\iint\limits_{H_i(S)} z\,dxdy = \frac{128 r_i^7}{3} \oint\limits_{H(\Omega_i)} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)^3} +
$$

$$
+ \left(\frac{8r_i^5}{3} - \frac{z_i + r_i}{2} \right) \oint\limits_{H(\Omega_i)} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)^2} +
$$

$$
+ \frac{2r_i^3}{3} \oint\limits_{H(\Omega_i)} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)},
$$

where $H(\Omega_i)$ is boundary of Ω_i. Therefore, $H(\Omega_i)$ is generated by points of (t,s) plane satisfying

$$
a_j^i(t^2 + s^2) + b_j^i t + c_j^i s + d_j^i = 0, \quad \text{for some } j \in \Psi_i. \quad (11)
$$

Eq. (11) expresses either circle ($a_j^i \neq 0$) or line ($a_j^i = 0$). Hence, $H(\Omega_i)$ consists of parts of circles or parts of lines. It is easy to see that $a_j^i = 0$ geometrically describes the following extreme situation when the surface of j-th sphere passes the *North Pole* of $i-$th sphere.

4. COMPUTATION OF $\oint\limits_{H(\Omega_I)} \frac{TDS - SDT}{(T^2 + S^2 + 4R_I^2)^K}$

Let $N_i \subset \Psi_i$ be the set of order numbers of the spheres which intersect the i-th sphere, and Λ_j^i be the number of arcs which generate the boundary of Ω_i and descend from the j-th sphere and all arcs $C_{j,\lambda}^i$ together create the boundary of Ω_i whereby $C_{j,\lambda}^i$ are oriented positively with respect to Ω_i provided that $a_j^i < 0$ and negatively otherwise. The image of each arc $C_{j,\lambda}^i$ is part of a circle or a line. Then we have

$$
\oint\limits_{H(\Omega_i)} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)^k} = \sum_{j\in N_i} \sum_{\lambda=1}^{\Lambda_j^i} \oint\limits_{C_{j,\lambda}^i} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)^k}, \quad (12)
$$

$k = 1, 2, 3$.
For the simplicity, in what follows we drop the upper index i. To compute the volume $V(S)$ it is sufficient to give formulas for the following curve integrals:

$$
J_k = \oint\limits_{C_{j,\lambda}} \frac{tds - sdt}{(t^2 + s^2 + 4r_i^2)^k}, \qquad k = 1, 2, 3.
$$

There are two possibilities. If $C_{j,\lambda}$ is the circle arc given by (11) (where $a_j \neq 0$) then $C_{j,\lambda}$ is parametrized as follows:

$$
\begin{aligned} t &= t_0 + r_0 \cos\varphi \\ s &= s_0 + r_0 \sin\varphi \end{aligned} \quad \text{for} \quad \varphi \in \langle \alpha_{j,\lambda}; \beta_{j,\lambda} \rangle. \quad (13)
$$

We admit only positive values of $\alpha_{j,\lambda}$ and $\beta_{j,\lambda}$. After some computations we arrive to the following relations.

$$
J_1 = \frac{\beta_{j,\lambda} - \alpha_{j,\lambda}}{2} + \frac{r_0^2 - A}{2} I_1, \quad J_2 = \frac{1}{4} I_1 + \frac{r_0^2 - A}{4} I_2,
$$

$$
J_3 = \frac{1}{8} I_2 + \frac{r_0^2 - A}{8} I_3,
$$

where

$$
I_k = \int\limits_{\alpha_{j,\lambda}}^{\beta_{j,\lambda}} \frac{d\varphi}{(A + B\cos\varphi + C\sin\varphi)^k}, \qquad k = 1, 2, 3
$$

with

$$
B = t_0 r_0, \ C = s_0 r_0, \ A = \frac{4r_i^2 + t_0^2 + s_0^2 + r_0^2}{2}
$$

and

$$
t_0 = -\frac{b_j}{2a_j}, \quad s_0 = -\frac{c_j}{2a_j},
$$

$$r_0 = \sqrt{\frac{(b_j)^2 + (c_j)^2 - 4a_j d_j}{4a_j^2}}.$$

If we denote

$$D = A^2 - B^2 - C^2$$

then one can verify that for the case when

$$\beta_{j,\lambda} - \alpha_{j,\lambda} < 2\pi$$

the following formulas hold

$$I_1 = \frac{2}{\sqrt{D}}\left(\frac{\pi}{2} - \arctan\frac{Y}{\sqrt{D}\sin\frac{\beta_{j,\lambda}-\alpha_{j,\lambda}}{2}}\right),$$

where

$$Y = A\cos\frac{\beta_{j,\lambda}-\alpha_{j,\lambda}}{2} + B\cos\frac{\alpha_{j,\lambda}+\beta_{j,\lambda}}{2} +$$

$$+ C\sin\frac{\alpha_{j,\lambda}+\beta_{j,\lambda}}{2}$$

$$I_2 = \frac{1}{A^2-B^2-C^2}\left(\left.\frac{-B\sin x + C\cos x}{A+B\cos x + C\sin x}\right|_{\alpha_{j,\lambda}}^{\beta_{j,\lambda}} + AI_1\right),$$

$$I_3 = \frac{1}{2D}\left(\left.\frac{-B\sin x + C\cos x}{(A+B\cos x + C\sin x)^2}\right|_{\alpha_{j,\lambda}}^{\beta_{j,\lambda}}\right) +$$

$$+ \frac{1}{2D}\left(\left.\frac{\frac{-B}{A}\sin x + \frac{C}{A}\cos x}{A+B\cos x + C\sin x}\right|_{\alpha_{j,\lambda}}^{\beta_{j,\lambda}}\right) + \frac{2A^2+B^2+C^2}{2AD}I_2.$$

For the case when $\alpha = 0$ and $\beta = 2\pi$ the integrals I_1, I_2, I_3 are equal:

$$I_1 = \frac{2\pi}{D^{1/2}}, \qquad I_2 = \frac{2\pi A}{D^{3/2}}, \qquad I_3 = \frac{\pi(2A^2+B^2+C^2)}{D^{5/2}}.$$

Now, we consider the second case, namely the extreme situation when $C_{j,\lambda}$ is a line segment with the first point $A = [t_0, s_0]$ and ending point $B = [t_1, s_1]$. In view of (11) assume that $C_{j,\lambda}$ lies in the line $b_j t + c_j s + d_j = 0$. Then we can describe $C_{j,\lambda}$ as follows

$$\begin{aligned} t &= t_0 + kc_j \cdot \varphi \\ s &= s_0 - kb_j \cdot \varphi \end{aligned} \qquad \text{for} \quad \varphi \in \langle 0; 1\rangle, \qquad (14)$$

where $k = \frac{t_1-t_0}{c_j} = \frac{s_1-s_0}{-b_j}$. In this case

$$J_1 = \frac{kd_j}{C}\widetilde{I_1}, \qquad J_2 = \frac{kd_j}{C^2}\widetilde{I_2},$$

$$J_3 = \frac{kd_j}{4(AC-B^2)}\left(\frac{B+C}{(C+2B+A)^2} - \frac{B}{A^2} + \frac{3}{C}\widetilde{I_2}\right),$$

where

$$\widetilde{I_1} = \frac{C}{\sqrt{AC-B^2}}\left(\arctan\frac{B+C}{\sqrt{AC-B^2}} - \arctan\frac{B}{\sqrt{AC-B^2}}\right),$$

$$\widetilde{I_2} = \frac{C^2}{2(AC-B^2)}\left(\frac{B+C}{C+2B+A} - \frac{B}{A} + \widetilde{I_1}\right)$$

with

$$A = 4r_i^2 + t_0^2 + s_0^2, \quad B = k(c_j t_0 - b_j s_0), \quad C = (b_j)^2 + (c_j)^2.$$

In the case when Ω_i is unbounded, but $\Omega_i^c = R^2 - \Omega_i$ is bounded we can use the following equality

$$16r_i^4 \iint\limits_{\Omega_i}\left(\frac{\partial Q(t,s)}{\partial t} - \frac{\partial P(t,s)}{\partial s}\right)dtds +$$

$$+ 16r_i^4 \iint\limits_{\Omega_i^c}\left(\frac{\partial Q(t,s)}{\partial t} - \frac{\partial P(t,s)}{\partial s}\right)dtds = \frac{4}{3}\pi r_i^3,$$

for computing of surface integral in (10).

Provided that neither Ω_i nor Ω_i^c are bounded then the boundary of Ω_i may consist also a part of circle with infinite radius or part of half line. In this case we shall use the following formulas.

$$\lim_{r\to\infty}\int\limits_{C(r)}\frac{tds-sdt}{t^2+s^2+4r_i^2} = \gamma, \quad \lim_{r\to\infty}\int\limits_{C(r)}\frac{tds-sdt}{(t^2+s^2+4r_i^2)^j} = 0,$$

$$(15)$$

for $j = 2, 3$ and where $C(r)$ is a positively orientated circle part with the fixed center point accordant to the radius r and the angle γ.

Let $C_{j,\lambda}$ be the half line segment with starting point (t_0, s_0) which lies in line $p: b_j t + c_j s + d_j = 0$. Denote

$$A = 4r_i^2 + t_0^2 + s_0^2, \quad B = k(c_j t_0 - b_j s_0), \quad C = (b_j)^2 + (c_j)^2$$

and

$$I_1 = \frac{C}{\sqrt{AC-B^2}}\left(\frac{\pi}{2} - \arctan\frac{B}{\sqrt{AC-B^2}}\right).$$

Then

$$J_1 = \frac{kd_j}{C}I_1, \quad J_2 = \frac{kd_j}{2(AC-B^2)}\left(I_1 - \frac{B}{A}\right),$$

$$J_3 = \frac{kd_j}{4(AC-B^2)}\left(\frac{3C}{2(AC-B^2)}\left(I_1 - \frac{B}{A}\right) - \frac{B}{A^2}\right),$$

$$(16)$$

where $k = 1$ in case when the orientation of half line is in direction of vector $(c_j, -b_j)$ and $k = -1$ in case when the orientation of half line is in direction of vector $(-c_j, b_j)$.

Remark 1 *Using the rotations of the whole molecule one can avoid the case of straight lines boundary parts of Ω_i. In this case, the boundary of Ω_i or Ω_i^c consists only of circular arcs.*

5. COMPUTATIONAL ASPECTS

Last sections describe the procedure which computes volume of overlapping spheres. In this section we will apply these results for construction of the algorithm and its computational complexity for computing $V(S)$.

Algorithm **Volume**
Input: $S_1, \cdots, S_n$
Output: $V(S) = V(\bigcup_{j=1}^{n} S_j)$
1. Compute $N_i, \Lambda_j^i, C_{j,\lambda}^i$
2. Orientate $C_{j,\lambda}^i$
3. Parametrize $C_{j,\lambda}^i$
4. Compute $J_k, I_k, k = 1, 2, 3$
5. Compute $V(S)$

Theorem 1 *Algorithm* **Volume** *works correct and terminates after $O(n^2)$ steps.*

Proof. Computational complexity of the algorithm is determines by step 1. But to compute elements of N_i and Λ_j^i for given $i \in \{1, \ldots, n\}$ ask for $O(n)$ steps. Then step 1 has complexity $O(n^2)$. Then each of steps has the best worst-case performance $O(n^2)$.
$\square$

Proposed analytical method is several times faster than numerical method established on division of molecules on small cubes. It can successfully run on parallel computers [2, 3].

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BIOGRAPHIES

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