Rotational molecular deformation of Ion selective channel protein that perforate excitable biological membrane.

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Geometric method has been introduced to calculate the change in the Van der Waals factor $1/r^7$ of the subunit of Acetyl choline sensitive channel on the excitable cellular membrane.

Key words. Acetyl choline sensitive channel, α helix, geometric analysis.

1.INTRODUCTION.

The biological channel on the excitable cellular membrane is composed of finite number of subunits which are also consisted of membrane perforating cylindrical polypeptides. The channel opening and closing are determined by the constitutional molecular structural changes in those cylindrical polypeptides. We have to make clear "changes in distribution of atoms or amino acids as assemblies of atoms during opening transition." We propose a geometric method for computation of the Van der Waals inter molecular force acting among all the amino acids molecules on the subunits of channel before and after the channel opening.

2.BIOPHYSICAL PROPERTIES OF CHANNEL.

Fig.1-a is a total structure of one Acetyl choline channel molecule. [1][2]. The members of these proteins are named by M1, M2, M3 and M4 helices [3] (Fig.1-b). The M2 helices face to the inner surface of the channel hole along their total length (2.5nm to 3.5nm) [4]. When the channel is closed (upper part of Fig.1-c), all the M2 helices kink (knee) at the middle region across the membrane [4]. The uppers part of the M2 helices slope in radial by 30 (θ a) degree toward the longitudinal axis of the channel [4]. Ten amino acid residues are arranged helically on the M2. The rising angle of the helical spin is ϕ=30 degree [5].

3. MODELING OF CHANNEL STRUCTURE AND ITS DEFORMATION.

We assume that all the atoms of one amino acid of the M2 helices are assembled as if they are point charges. We assume that ten point atoms locate spiral fashion by helical returning (Fig.2). Fig.2 is an YOo view of two M2 cylinder projected on an XZ plane. Upper parts of two adjacent M2 helices were projected on an XZ plane (Oo denotes the origin). θ a is the angle by crossing the inclined circular plane of the bottom of the first cylinder and the XY plane. ϕ is the rising angle of the projected swirl spin on an XZ plane. xn' is the projected position of point amino acid molecules line up helically on the M2 helix. The projected spiral organized point molecules on the second M2 cylinder were denoted by yn'.

3-A. LOCATIONS OF PROJECTED POINT ATOMS OF THE HELICAL STRIPE.

Fig.3 shows circular allocation of spirally organized point molecules that were projected on the bottom circular plane of the first M2 helix. θ c is the equivalent circumferential angle made by two adjacent helical point molecules. xn is the circumferential locations of the helical points around the bottom circle. xn''' is the projected xn' on the diameter O1C1X. We have

$$O1'X' = \sqrt{[(2a)^2 + (L/2)^2]} \quad ---(1)$$
$$O1x1'' = O1x10'' = a - a\cos(\theta c/2) \quad ---(2)$$

Fig.4. is a side view of the spirally allocated molecular points projected on an XZ plane. This figure shows locations of xn, xn',xn'',xn''' and xn*. xn' is a helical point on an XZ plane. xn'' is a projected point on the XY plane passing through the center C1'. xn* is position on the plane O1'. X components of distance from the center Oo to xn' are as

$$x1*Oo* = 2a\cos(\theta a)$$
$$+a\cdot O1x1''/\cos(\phi)\cos(\theta a + \phi) \quad ----(3)$$

2. Z components of distance from the central plane XY involving C1'Oo to xn' is calculated by using xn''.

$$x1'x1'' = a\sin(\theta a) - (a - a\cos(\theta c/2))$$
$$/\cos(\phi)\sin(\theta a + \phi) \quad ----(4)$$

3. Calculation of Y components requires a top view of the system. Fig.5 is a top view of the first cylinder which was looked down along the ZOo axis. We have

$$x3''x4'' = a - a\cos(\theta c) \quad -----(5)$$

3-B. DISTANCE BETWEEN POINT ATOMS ON HELICAL STRIPES OF TWO CYLINDERS.

X component of $x1y1 = x1''Oo - y1''' C2 ----(6)$

Y component of $x3y1 = x3''C1$
$$+ \text{y component of } Ooy1' \quad ----(7)$$

z component of $x1y1 = x1'x1'' + y3''Oo$
$$+ y3'y3''\cos(a) + y1''y1' \quad -----(8)$$

4. Ξ DEGREE ROTATION OF THE FIRST YLINDER AROUND THE ZO AXIS ON THE XYO PLANE.

The knees of the M2 helices were drawn near to the longitudinal axis of the channel. The upper and lower portions of the M2 helices fall remote from the axis. M2 helices are pushed apart from the center area of the channel [4]. During the opening reaction, all the M2 helices rotate around the central longitudinal axis of the channel by ξ (Fig 6). Z components do not change by the ξ rotation. An X component of the distance (xn,yn) after the ξ rotation is obtained by multiplying the factor of $\cos(\xi)$ on all the X components of the distance between (xn,yn). Calculation of Y component is more difficult (Fig.6). By observing along the ZOo axis, numbering of the helical points of the first cylinder starts from x3. Thus,

$$x3'''xn'''/ x3'xn' = \cos(\phi) \quad \text{------(9)}$$
$$x* = a \tan(\pi/2 - \xi) \quad \text{-------(10) and}$$
$$y* = (a + x*) \sin(\pi/2 - \xi) \quad \text{-------(11)}$$

we have

$$z* = -y* + \sqrt{[a^2 \tan(\pi/2 - \xi)^2 + a^2]}$$
$$= -y* + a / \cos(\pi/2 - \xi) \quad \text{-----(12)}$$

Thus, the y component after ξ rotation is given by

$$x3'xn' \sin(\phi + \pi/2 - \xi) + z*$$
$$= x3'xn' \sin(\phi + \pi/2 - \xi)$$
$$\quad + a / \cos(\pi/2 - \xi) - (a + a \tan(\pi/2 - \xi))$$
$$\sin(\pi/2 - \xi) \quad \text{-----(13)}$$

where $x3'xn' = x3'''xn'''/\cos(\phi)$

5. VAN DER WAALS ENERGY AND FACTOR

There are many formulas for Van der Waals forces depending on the structures [6]. For example at an atom-surface interaction, the Van der Waals force is $w= - C\pi \rho /6r^3$ where ρ is the density of atoms in a plane surface [6]. For spherical molecules with their diameter large than 0.5nm, $w=-Ar1r2/(6D(r1+r2))$ where D is the nearest distance between the surfaces of two spheres [6].The inverse six power law holds only for two structure less point atoms or molecules[6].

Magnitude of an induced electrical filed of a dipole in the vacuum by the interaction between polar and non polar molecules can be expressed by [6]

$$E = u (1 + 3\cos^2(\theta))^{1/2}/(4\pi \varepsilon o \varepsilon r r^3) \quad \text{----(14)}$$

where u is the fixed permanent dipole. θ is a cross angle between the central axis of polarized and polarizing molecules, εr is relative permitivity, εo is in vacuum. The interaction energy is given by integrating electrical force F [6]

$$w = \int F dr = \int (\alpha o E dE /dr) dr \quad \text{----(15)}$$
$$= -1/2 \alpha o E^2 = -u^2 \alpha o (1 + 3\cos^2(\theta))$$
$$/[2(4\pi \varepsilon o \varepsilon r)^2 r^6] \quad \text{----------(16)}$$

where αo is the electric polarizability of non polar molecule. Since the angular expectation value of $\cos^2(\theta) = 1/3$, we have finally

$$w(r)= -u^2 \alpha o /[(4\pi \varepsilon o \varepsilon r)^2 r^6] \quad \text{----(17)}$$

London [6] provided following formula for energy by two interacting atoms or molecules

$$w(r)= -3/4 \alpha o^2 h \nu /[(4\pi \varepsilon o)^2 r^6] \quad \text{---(18)}$$

According to the McLachlan theory [6], the Van der Waals energy between two spherical molecules in the solvent takes the form of

$$w(r)=-a1^6/r^6[3kT((\varepsilon r,1(0)- \varepsilon r,3(0))/(\varepsilon r,1(0)+2 \varepsilon r,3(0))]^2+\sqrt{3} h \nu e/4 (n1^2-n3^2)^2/(n1^2+2n3^2)^{3/2}]--(19)$$

$\varepsilon r,1$, $\varepsilon r,3$, are the dielectric permitivities of the interacting spherical molecules and solvent. ν e is the absorption frequency of molecules and solvent at ultra violet spectrum, nm is the reflection coefficient given by $nm=\sqrt{[\varepsilon r,3(\nu vis)]}$ where ν vis is the absorption frequency at the visible wave spectrum region [6]. We assumed that all the physical parameters are constant during structural changes. The force can be calculated by differentiating the energy with respect to r. Thus the present paper call $1/r^7$ as the Van der Waals factor instead of force or energy.

6. COMPUTED RESULTS.

Fig.7 shows computed Van der Waals factor c/r^7 timed by the factor 10^{-5} when the channel is closed (ξ =0). Values of $1/r^7$ were shown as a function of (θ a) and rising angle (ϕ). The decrease was sensitive to the slope of the M2 helix.

7.SIGNIFICANCE FOR ORGANIC MOELCULAR ELECTRONICS AND APPLICATION.

Most of the biological channel molecules on excitable membranes such as neural cell and cardiac muscle have subunits which are composed of membrane perforating polypeptides. The coordinated and concerted structural changes during the channel state transition from close to open structures can be described by the "Allosteric" properties. These features are characterized by energy and time saving evolution of the system. Starting from a local minimum molecular structural change, the deformation extends to an entire part of one channel molecule with magnification. The successive structural changes are accelerated. Such process save the energy for molecular deformation. The accelerated reform can be regarded as the time minimum, the shortest time controlled system. In the material science, such properties will be available for creating solid state new electronic device and material. For example, functions of some chemical sensors or filters will be improved their noise selectivity and fast signal transmission properties by be inspired of these biological Allosteric properties. To develop such new material, the present work will be available for basic approach to analyze the potential change during the deformation of the Allosteric molecules.

8. CONCLUSION.

We developed a geometric method to calculate the change in the intermolecular potential before and after the deformation for opening channel state transition.

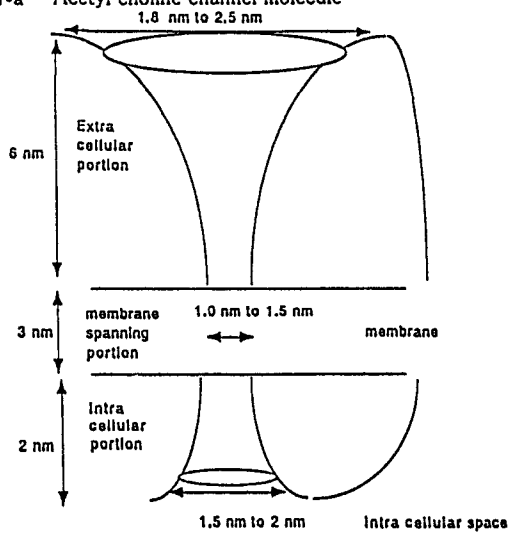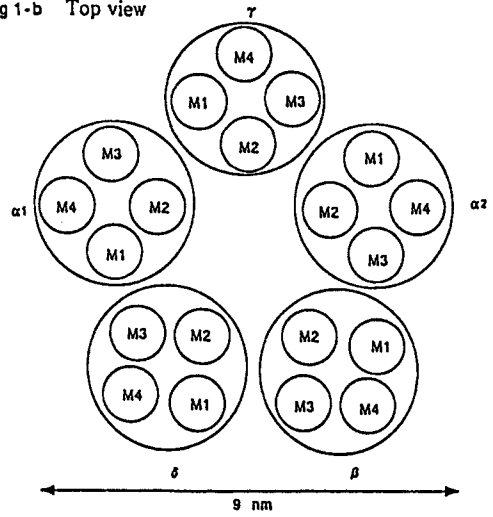Fig 1-a   Acetyl choline channel molecule

Fig 1-b   Top view

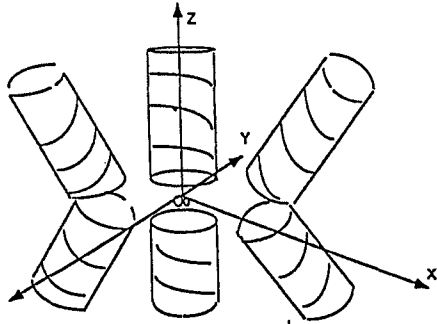Fig 1-c   Deformation of M2 helices
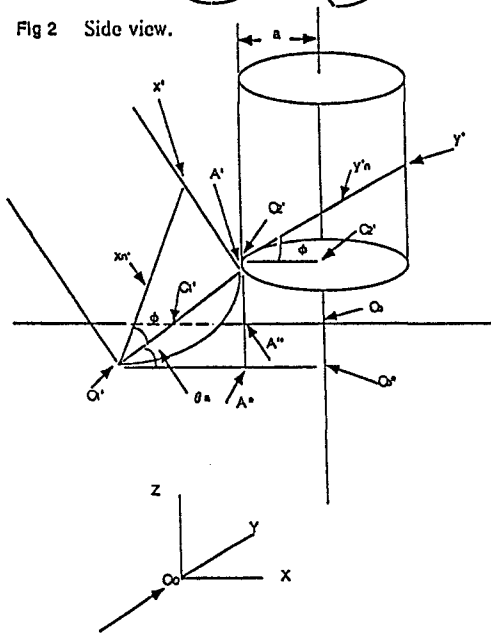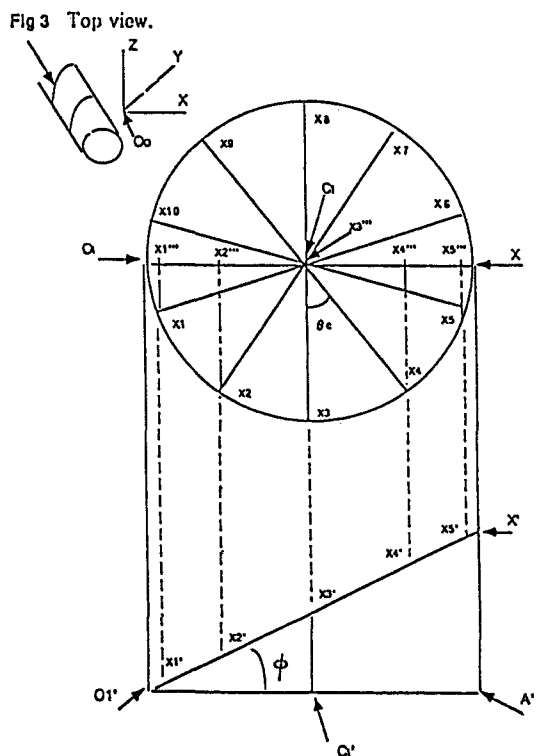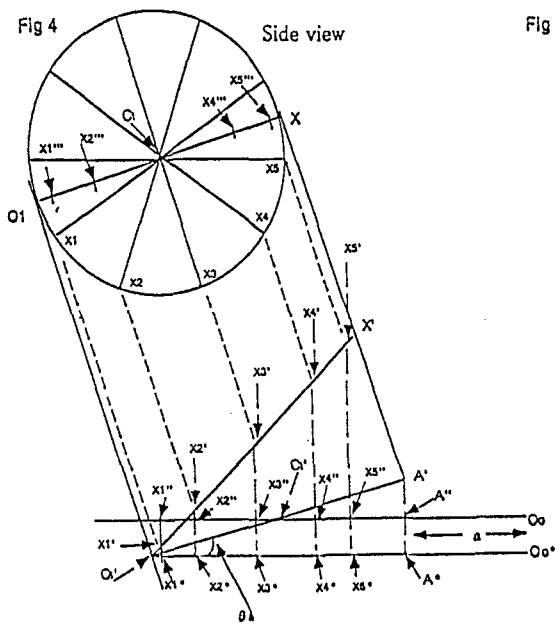

Fig 2   Side view.

Fig 3   Top view.

Fig 4   Side view

Fig 5   Top view of the first M2 observed from ZOo.
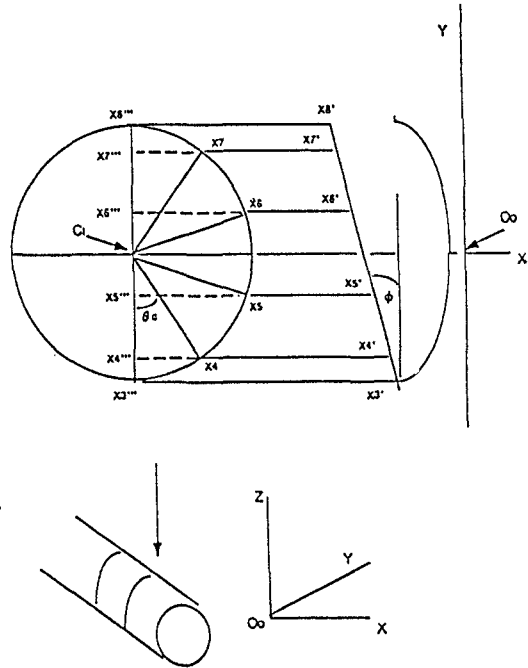
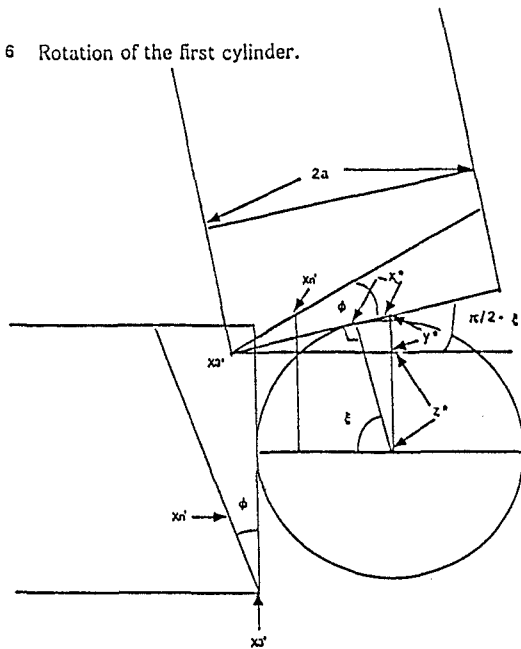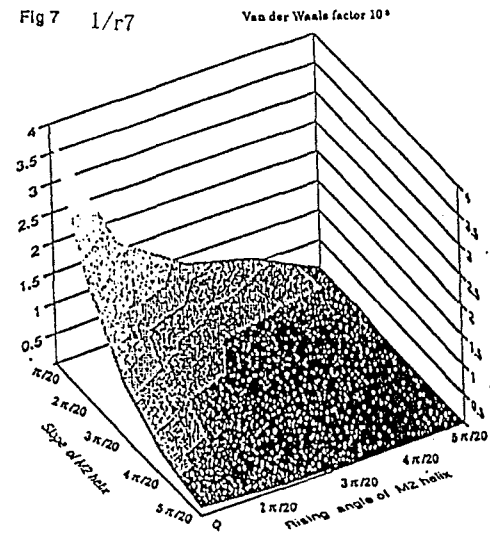Fig 6   Rotation of the first cylinder.

Fig 7   1/r7

Van der Waals factor 10⁴

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