MODEL GEOMETRY FOR HIV-1 AND -2

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Summary. A model geometry for the HIV-1 and -2 viruses is proposed based on electron microscopic observations. Standard geometric shapes are employed to describe the surface membrane, stalk (glycoprotein 41), and knob (glycoprotein 120) of the virus. Based on approximate dimensions for certain features of the virus estimates are provided for viral surface area and volume in both budding and mature stages, stalk-knob assembly surface area and volume, surface membrane area, surface membrane radius, and the ratio for surface area in the budding and mature virus. Such estimates may be useful in the quest for compounds that inhibit virus replication.

KEY WORDS. Retrovirus, AIDS virus, HIV virus, Viral Geometry, Model Geometry

1. Introduction. The human retroviruses HIV-1 and HIV-2 are known to be the etiological agents of acquired immune deficiency syndrome – a progressive, degenerative disease of the immune and central nervous system [1]. In 1981, reports of *Pneumocystic carinii* pneumonia among Los Angeles homosexuals marked the recognition of what has come to be known as AIDS, followed in 1984 by the discovery of the causal virus, and in 1985 serological tests for antibodies to the virus were developed and made available [2]. The viruses have been isolated in tissues and organs: blood lymphocytes, lymph nodes, bone marrow, brain tissue, cell-free plasma, saliva cells, semen, cerebrospinal fluid, and breast milk [3, 4].

The structure of the virus is known to be a spherical-like surface membrane, consisting of a lipid bilayer, studded with projections consisting of two glycoproteins [5, 7]. More particularly, the surface membrane is thought to have icosahedral symmetry and be studded with 72 projections arranged in a $T = 7$ laevo symmetry [6]. Each projection is made up of a stalk of glycoprotein 41 (GP 41) surmounted by a knob of glycoprotein 120 (GP 120)

[7]. No morphological differences between HIV-1 and HIV-2 strains have been detected [8]. The viral life span consists of two main phases-budding and mature; there seems to be a progressive loss of surface projections during the maturation phase [7]. Figure 1 depicts a structural model of the organization of HIV with some of the projections missing in (a) while (b) shows a detail of the stalk-knob assembly at the surface with approximate dimensions.

It would be useful to have measurements for the surface area and volume of these viruses as a support for investigators who are searching for anti-viral agents and vaccines. These surface area and volume estimates could be crucial factors in designing therapies or viral inhibitors; this rationale based on the assumption that compounds that inhibit virus replication will arrest the disease. A model geometry for the virus will allow the estimation of surface area and volume for a typical virus, in both budding and mature phases, and also yield an estimate for the surface membrane diameter in the process.

2. Model Geometry. The model geometry, upon which all subsequent work is herein based, will consist of a spherical surface membrane with circular cylindrical stalks representing glycoprotein GP 41, each stalk surmounted by an oblate spheriod knob representing glycoprotein GP 120. Figure 1 shows such a model geometry. This is, of course, an idealization, albeit a necessary one if estimates are to be made. We let the number of stalk-knob assemblies on the viral surface membrane be given by N, where N can vary from 0 to 72 representing the completely mature to budding virus (and those between these two phases). Recall that an icosahedron consists geometrically of 20 equilateral triangular faces, 30 edges, and 12 vertices and has 5-, 3-, and 2-fold axes of rotational symmetry or (532) symmetry. It is thought to be the most efficient form of packing or the optimum design [9]. The triangulation number $T = 7$ associated with laevo symmetry allows for 72 capsomeres and will be used here to describe HIV. For ease of calculation a spherical approximation to the icosahedron, the sphere being circumscribed, will be used.

3. Formulary. The well-known formulas for surface area and volume of a sphere of radius r_m and $S_m = 4\pi r_m^2$ and $V_m = \frac{4}{3}\pi r_m^3$, respectively. The stalk as a right-circular cylinder has surface area and volume expressions $S_s = 2\pi rh$ and $V_s = \pi r^2 h$, respectively,

where r is the radius and h is the height of the stalk. Each knob considered as an oblate spheroid has surface area

$$S_k = 2\pi a^2 + \frac{2\pi a c^2}{(a^2 - c^2)^{\frac{1}{2}}} \left\{ \ln \frac{c(a^2 - c^2)^{\frac{1}{2}} + ac}{c^2} \right\} \tag{1}$$

and volume

$$V_k = \frac{4}{3}\pi a^2 c \ , \tag{2}$$

where a and c are the semi-major and minor axes of the spheroid, respectively. When the total surface area for the virus is found, we must account for the fact that the ends of the stalk actually cover some of the membrane and knob surface area; this covered area will not be counted in the total surface area. Total volume calculation is not so affected.

The formula for the combined surface area of a single stalk-knob assembly is given by

$$S_{s-k} = 2\pi r h + 2\pi a^2 + \frac{2\pi a c^2}{(a^2 - c^2)^{\frac{1}{2}}} \left\{ \ln \frac{c(a^2 - c^2)^{\frac{1}{2}} + ac}{c^2} \right\} - \pi r^2 \ , \tag{3}$$

while the volume is given as

$$V_{s-k} = \pi r^2 h + \frac{4}{3}\pi a^2 c \ . \tag{4}$$

The entire virus has a total surface area

$$S_{\text{total}} = 4\pi r_m^2 + N \Bigg\{ 2\pi r h + 2\pi a^2 + \frac{2\pi a c^2}{(a^2 - c^2)^{\frac{1}{2}}} \cdot \left[\ln \frac{c(a^2 - c^2)^{\frac{1}{2}} + ac}{c^2} \right] - 2\pi r^2 \Bigg\} \ , \tag{5}$$

when N stalk-knob assemblies are present. This expression composed of the area of the spherical surface membrane plus the areas of the N stalk-knob assemblies corrected for

overlap on the sphere and underside of the knob. The volume for the entire virus is given by

$$V_{\text{total}} = \frac{4}{3}\pi r_m^3 + N\big(\pi r^2 h + \frac{4}{3}\pi a^2 c\big) \ , \tag{6}$$

where N is the number of stalk-knob assemblies on the surface. This volume formulation is composed of the surface membrane volume plus the volumes of the N stalk-knob assemblies. These formulas, equations (5) and (6), depend on N and so one must have an idea about how many stalk-knob assemblies are present.

4. Geometric Feature Estimates. Estimates can now be given for the stalk-knob assembly surface area and volume, surface membrane radius, total surface area, total volume, uncovered surface membrane area, and the ratio of surface area for the budding and mature virus. Reports in the literature give measurements which are useful in the estimates mentioned above [7, 8]. With estimates of 3.5–4 nanometers (nm) for the radius and 4–7 nm for the height of the stalk, the surface area of a single stalk is 87.9–175.8 nm^2 and the volume is 153.9–351.7 nm^3. The knob is calculated to have semi-axes lengths of $a = 7.5$ nm and $c = 2.5$ nm [7]; these measurements then give surface area of 426.8 nm^2 and volume of 582.0 nm^3 for a single knob. The total surface area for N stalk and knob assemblies is then given by $N(476.3) - N(552.6)\text{nm}^2$, and the volume has the range of values $N(743.0) - N(940.9)\text{nm}^3$. The diameter of the entire virus is estimated as 100–120 nm, including the protruding stalks and knobs [8]. Subtracting from this overall diameter the heights of two stalk-knob assemblies on opposite sides, the diameter of the surface membrane is estimated as 76–96 nm; this implies a surface membrane radius estimate of 38–48 nm. The total surface area of the virus including N stalk-knob assemblies is found to be from $18136.6 + N(437.8)$ to $28938.2 + N(502.4)\text{nm}^2$. The total volume including N stalk-knob assemblies is from $229730.8 + N(743.0)$ to $463011.8 + N(940.9)\text{nm}^3$. The uncovered surface membrane area is that area on the membrane that is not covered by the bases of the stalks. It is given by the range of values from $18136.6 - N(38.5)\text{nm}^2$ to $28938.2 - N(50.2)\text{nm}^2$. All of the above estimates that contain the number of stalk-knob assemblies N may be used with any integral value of N between 0 and 72.

If it is assumed that when $N = 72$, the virus is in the budding stage and when $N = 0$, the virus has lost all of its stalk-knob assemblies and is in the mature stage, then their surface areas can be compared. The surface area of the budding virus is $49658.2 - 65111.0\text{nm}^2$ while that of the mature virus is $18136.6 - 28938.2\text{nm}^2$. These measurements indicate that the budding virus has approximately 2.7 to 2.3 times more surface area than a mature virus that has lost all of its surface projections.

5. Discussion. The model geometry and estimates drawn therefrom are results which hopefully will be useful to investigators as they offer a standard for comparison and further quantitative work. I realize that the accuracy of these estimates can be no better than the accuracy of the dimensions upon which they are based, however as first approximations they can hopefully serve a useful purpose.

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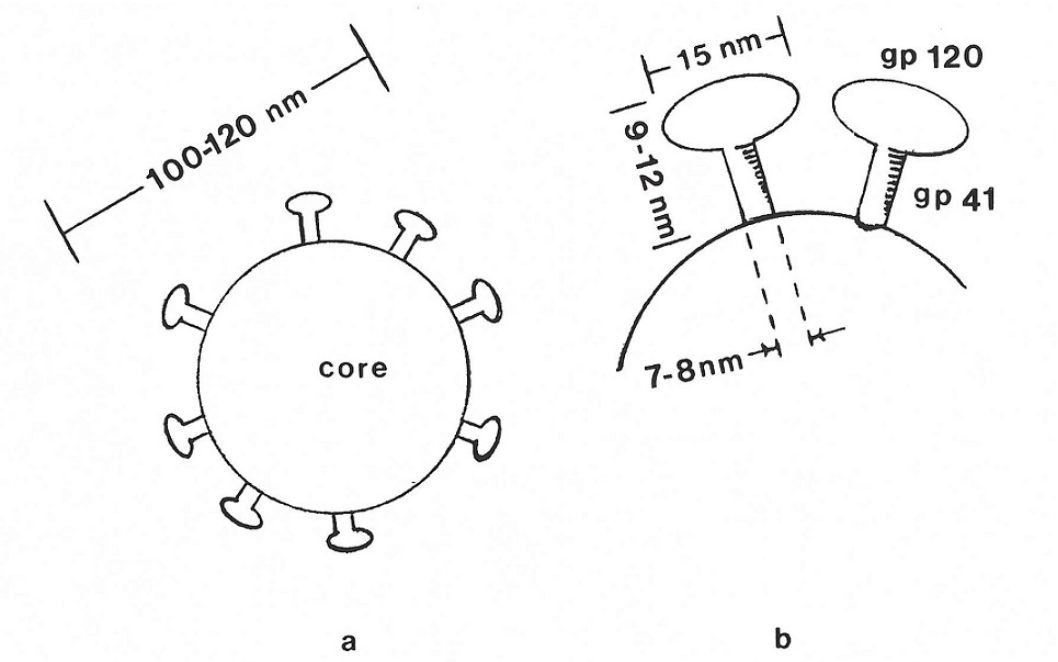

Figure 1.