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Deformation of toroidal DNA condensates under surface stress

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Abstract. – A qualitative rule is formulated for the shape deformation of DNA condensates, in which the surface stresses are balanced against bending forces. A quantitative analysis is presented for toroidal globules. Low surface tensions lead to ideal tori, high tensions give rise to compact toroids with thin inner tubes. A qualitative discussion is given of Laemmli's experiments on globules of monomolecular DNA.

The equilibrium collapse of a flexible chain is reasonably well formalized and understood [1]-[3]. Rather, the reverse is true when the chain is stiff and a persistence segment is highly anisometric, the all-important prototype being double-stranded DNA. Elasticity, orientation-translation coupling, the disparate Boltzmann weighting of repulsive and attractive forces [4], and the possibilities of complicated topologies and shapes of a collapsed globule, all conspire to make an *a priori* theory formidable, even at a self-consistent field level. Accordingly, one obvious simplification has been to guess the qualitative structure of such a globule on both local and global levels [5]-[10].

On the experimental side, the condensation of DNA into globules has been avidly studied for some time. It may be induced by a simple salt together with a neutral polymer like polyethylene oxide (PEO) soluble in aqueous solution [11]-[15]. A qualitative mechanism based on osmotic pressure is trivially clear, but a quantitative theory is another matter [7],[9]. Considerably more obscure is how DNA is condensed by multivalent cations [8],[16]-[19]: is the attraction caused by van der Waals forces [20] or by correlated cations [21]?

Here, we would like to focus less on the mechanism of the DNA condensation itself and more on the likely generic features of the globular shape. As we have argued previously [9], the packing within a globule *beyond a minimum size* is determined mainly by extensive energy contributions whereas its shape is sensitive to non-extensive higher-order terms. In effect, the appropriate thermodynamic potential Ω of a globule may be expressed schematically as

$$\Omega \;=\; F_{\rm bulk} \;+\; \Delta F\,, \tag{1}$$

where the extensive "bulk" free energy is proportional to the globular volume V or the contour length L of the DNA and all other terms are lumped together in ΔF, which generally is a functional of the shape h and the DNA density ρ. Next, we assume the globule is homogeneous enough so that an average spacing $a \sim (V/L)^{1/2}$ between DNA helices is a meaningful quantity. Then, it is simply computed from

$$\frac{\partial \Omega}{\partial V} \;=\; 0 \approx \frac{\partial F_{\rm bulk}}{\partial V}\,, \tag{2}$$

since the higher-order terms i must scale as V^{α_i}, with $\alpha_i < 1$ (for instance, the surface energy may scale as $V^{2/3}$ though not necessarily). The globular shape and density are now determined by $\delta\Delta F/\delta h = 0$ and $\delta\Delta F/\delta\rho = 0$ at fixed a. Such a scheme is expected to be fairly independent of the details of the DNA condensation itself, especially when we are concerned with the collapse of a single macromolecule. We have to be wary of multimolecular aggregation, for eq. (1) may then break down.

We can progress a bit further because we know that globular DNA is often close-packed [8],[11]-[13],[16]-[18] so it must behave at least like a fluid with minor density fluctuations. Hence, any non-uniform density contribution to ΔF should be small although there may be substantial surface effects. Furthermore, the persistent electrostatic repulsion between helices, even at high salt and with multivalent cations present, makes a complete collapse to a rigid solid unlikely. Thus, if the globular matter is always fluid, elasticity is superposable because DNA rearranges by sliding upon deformation of a condensate. On the whole, for a tightly wound globule shaped roughly like a torus or ellipsoid and characterized by, say, two radii of curvature R_1 and R_2, with $R_1 = \mathrm{O}(R_2) = \mathrm{O}(V^{1/3})$, we have the following leading contributions to ΔF: a bending energy ([1]) scaling as

$$\Delta F_{\rm b} \;\approx\; \frac{k_{\rm B}T\; P\; L}{R_1^2}\,, \tag{3}$$

where P is the DNA persistence length, and a necessarily positive surface energy, a sum over all surface terms, proportional to a surface tension σ (conveniently scaled by $k_{\rm B}T$, with $k_{\rm B}$ Boltzmann's constant and T the temperature)

$$\Delta F_{\rm s} \;\approx\; k_{\rm B}T\;\sigma\;V^{\frac{2}{3}}\,. \tag{4}$$

The surface and bending forces are antagonistic with respect to the globular shape [7], [9], the surface tension coming into play when a dimensionless parameter α is of order unity,

$$\alpha \;\equiv\; \frac{\sigma\; V^{\frac{1}{3}}\; a^2}{P}\,. \tag{5}$$

Various higher-order terms analogous to those discussed in ref.[9] may be disregarded. For instance, interhelix interactions —whether the fluid is hexagonal [9] or nematic (cholesteric) [22], [23]— do not alter the basic form of eq. (3).

We now investigate the import of surface forces on globular shape for one specific topology, the DNA toroid having axial symmetry. In cylindrical coordinates, a toroid of arbitrary though sufficiently regular cross-section may be defined by a curve $h(r)$ in the (r, z)-plane, where we choose the toroid axis to coincide with the z-axis (see fig. 1). The directrix of the DNA fluid

([1]) We neglect possible anomalous inner regions of minute volume but high curvature. These may appear if $\alpha \gg 1$.

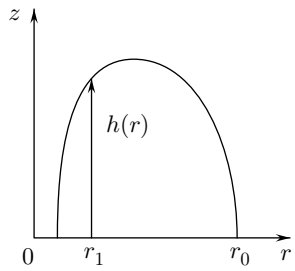

Fig. 1. – The toroidal coordinates.

is perpendicular to the plane. The bending energy is given by

$$\frac{\Delta F_{\rm b}}{k_{\rm B}T} \;=\; \frac{2\pi PL}{V}\int_{r_{\rm i}}^{r_{\rm o}} {\rm d}r\;\frac{h}{r}\,, \tag{6}$$

where $h(r)$ is assumed to be a single-valued, continuous and continuously differentiable function of r defined between the inner and outer radii, $r_{\rm i}$ and $r_{\rm o}$ (fig. 1). We express the surface energy as

$$\frac{\Delta F_{\rm s}}{k_{\rm B}T} \;=\; 4\pi\sigma\int_{r_{\rm i}}^{r_{\rm o}} {\rm d}r\;r\;\left[1\;+\;(h')^2\right]^{\frac{1}{2}}\,, \tag{7}$$

with $h' \equiv {\rm d}h/{\rm d}r$. As we argued above, we have to minimize $\Delta F = \Delta F_{\rm b} + \Delta F_{\rm s}$ at a fixed volume V

$$V \;=\; 4\pi\int_{r_{\rm i}}^{r_{\rm o}} {\rm d}r\;h\;r\,, \tag{8}$$

so it is convenient to scale $r \equiv lR$ and $h \equiv lH$ by $l \equiv V^{1/3}$. Accordingly, we minimize the functional g

$$g \;\equiv\; 4\pi\int_{R_{\rm i}}^{R_{\rm o}} {\rm d}R\;L[R, H(R), H'(R)]\,, \tag{9}$$

$$L \;\equiv\; HR^{-1}\;+\;\alpha_{\rm t}R\left[1+(H')^2\right]^{\frac{1}{2}}\;-\;\Lambda HR\,, \tag{10}$$

$$\alpha_{\rm t} \;\equiv\; \frac{2\sigma l^4}{LP}\,, \tag{11}$$

where we have introduced the Lagrange multiplier Λ, which can be shown to be positive. Note that the dimensionless coupling constant $\alpha_{\rm t}$ is identical with α (eq. (5)) to within a numerical constant. The Euler-Lagrange equation after rearrangement yields

$$H(R) \;=\; D + \int_{R_{\rm i}}^{R} {\rm d}R\;\frac{W}{\left[1-W^2\right]^{\frac{1}{2}}}\,, \tag{12}$$

with

$$W(R) \;=\; \alpha_{\rm t}^{-1}\left[\frac{\ln R}{R} - \frac{\Lambda R}{2} + \frac{C}{R}\right]\,. \tag{13}$$

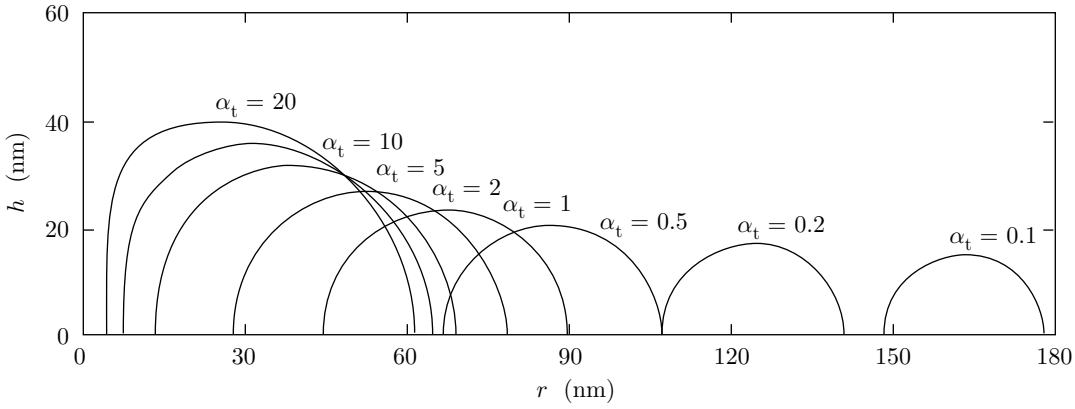

Fig. 2. – Cross-sections of a toroidal condensate for various values of α_t, calculated from eq. (12) with $L = 5.1 \cdot 10^4$ nm and $V = 7.1 \cdot 10^5$ nm^3. Because of symmetry, only the upper halves are shown.

There are now five integration constants R_i, R_o, Λ, C and D in accordance with five boundary conditions: $H(R_i) = H(R_o) = 0$, $H'(R_i) = \infty$, $H'(R_o) = -\infty$ and the volume constraint. In the limit $\alpha_t \ll 1$, it is not difficult to show analytically that H asymptotes towards a semicircular cross-section as it should. The best numerical approach to solving eq. (12) is by starting with some value for $\alpha_t \ll 1$ when initial estimates can be given [9]

$$4\,[R_o - R_i] \;\approx\; \alpha_t \;\; [R_o + R_i]^2 \tag{14}$$

and proceeding for incrementally larger values of α_t.

In fig. 2 we show representative cross-sections $h(r)$ for T4 DNA of contour length $L = 5.1{\cdot}10^4$ nm and persistence length $P = 50$ nm enclosed in a toroidal volume $V = 7.1{\cdot}10^5$ nm^3. For α_t much smaller than unity, the toroid is slender and the cross-section is almost circular as we expect. In this regime, an analytical scheme adapted to the model at hand [9] compares well with our numerical analysis. When α_t is much larger than unity, large deviations from circularity occur. The high surface tension forces the toroid to be compact so as to minimize its surface area. But this is offset in an inner region ($r = \mathrm{O}(r_i)$) where very high elastic forces tend to flatten the toroid in one direction forming a thin tube (fig. 2).

In a previous paper [9] we addressed the condensation of one DNA molecule into a hexagonally packed toroidal globule under the influence of a semidilute polymer. Scaling theory was used to estimate the osmotic pressure $\Pi_p \approx k_B T \xi^{-3}$ and the scaled surface tension $\sigma \approx \xi^{-2}$, where ξ is the correlation length, both in the bulk and in the depletion layer. However, since then we have come to suspect the quantitative applicability of the latter theory to a popular water-soluble polymer like PEO ([2]). For instance, using a Kuhn length of 1.2 nm, we obtain a scaling estimate for the osmotic pressure of order 0.1 bar at a PEO concentration of 100 g/l which compares unfavourably with an experimental value of about 1.0 bar [26]-[28]. Even more startling is the fact that the correlation length is one order of magnitude less than one would anticipate [29]. Still, in the absence of surface tension measurements, we think that a heuristic scaling ansatz $\sigma \approx (\Pi_p / k_B T)^{2/3}$ with an experimental Π_p may still be of value in an analysis of DNA condensation (provided that the surface tension of DNA may be neglected [9]).

We emphasize that the pressure balance itself, as used earlier [9], is not in doubt. The variation of Bragg spacings for ψ condensates with PEO and NaCl concentrations was measured

([2]) Some authors argue that anomalous hydrogen bonding occurs, see, *e.g.*, [24], [25].

long ago [13], [30]. We calculate the relevant osmotic pressures from an empirical expression given by Parsegian *et al.* [27]. Although the ionic-strength dependence of the Bragg spacings is subject to some ambiguity [30], the resulting pressure-spacing curves agree fairly well with both those determined for undeformed liquid-crystalline DNA [31],[32] and those predicted theoretically [9], [33]. Hence, eq. (2) is borne out.

Strong multimolecular aggregation often seems concomitant with condensation [8], [13], [16]-[19], [34], though Laemmli [12] described the collapse of single DNA molecules. According to our computations (fig. 2), α_t would have to be close to 5 and σ close to 0.1 nm^{-2} in order to explain the dimensions of his T4 DNA collapsed by polylysine. Unfortunately, neither do we have an independent estimate for σ nor did Laemmli ascertain the precise shape of his globules. He also found ellipsoidal particles when DNA was condensed by a 100 g/l solution of PEO. Our discussion above would lead to $\sigma \approx 0.1$ nm^{-2} and so $\alpha = \mathrm{O}(1)$ from eq. (5) which is consistent with the fairly weak anisometry of Laemmli's ellipsoids. Clearly, future experiments will be necessary to shed more light on the physics of DNA condensates. One option for testing our predictions for the globular shapes is small-angle X-ray scattering in dilute solution: Ronto *et al.* [35] have forcefully argued that the structural organization of compact DNA can, in fact, be elucidated given some *a priori* information of a qualitative kind.

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