

Abstract

Pores of ion channels that follow the basic architecture of KcsA possess a hydrophobic region which changes its conformation between a wide pore, when open, to a narrower pore, when closed. Recent studies indicate that a hydrophobic pore can "gate" by capillary evaporation. With this mechanism water is expelled from the permeation pathway and ion flow is thereby stopped although the pore remains wider than the water or ion diameters. We study the connection between geometrical change of a hydrophobic pore and capillary evaporation to estimate the energetics of this gating mechanism in a realistic pore geometry, e.g. the energy it takes to remove the water from the pore and the force exerted by the water on the wall of the pore.

To this end we perform, in a first step, microscopic density functional theory (DFT) calculations, in which we focus on the density profile of water as capillary evaporation takes place. The

insight gained from these DFT calculations we transfer and exploit, in a second step, in our mesoscopic morphometric approach. In morphometry the free energy of a liquid confined in a pore is expressed by four terms that describe the geometry of the pore and corresponding thermodynamic coefficients. This separation of geometry and thermodynamics makes calculations very efficient so that effects due to change in geometry can be studied in depth. Both DFT and morphometry have been applied with great success in studies of the physics of confined fluids.

DFT: the White Bear Version of FMT

$$\Omega[\{\rho_i\}] = \mathcal{F}_{ex}[\{\rho_i\}] + \mathcal{F}_{id}(\{\rho_i\}) + \sum_i \int d^3r \rho_i(\mathbf{r}) (V_i(\mathbf{r}) - \mu_i)$$

with the excess free energy (over ideal gas)

$$\beta \mathcal{F}_{ex}[\{\rho_i\}] = \int d^3r' \Phi(\{n_\alpha(\mathbf{r}')\}) + \frac{1}{2} \int d^3r' \int d^3r'' \rho(\mathbf{r}') \rho(\mathbf{r}'') V_{sw}(|\mathbf{r}' - \mathbf{r}''|)$$

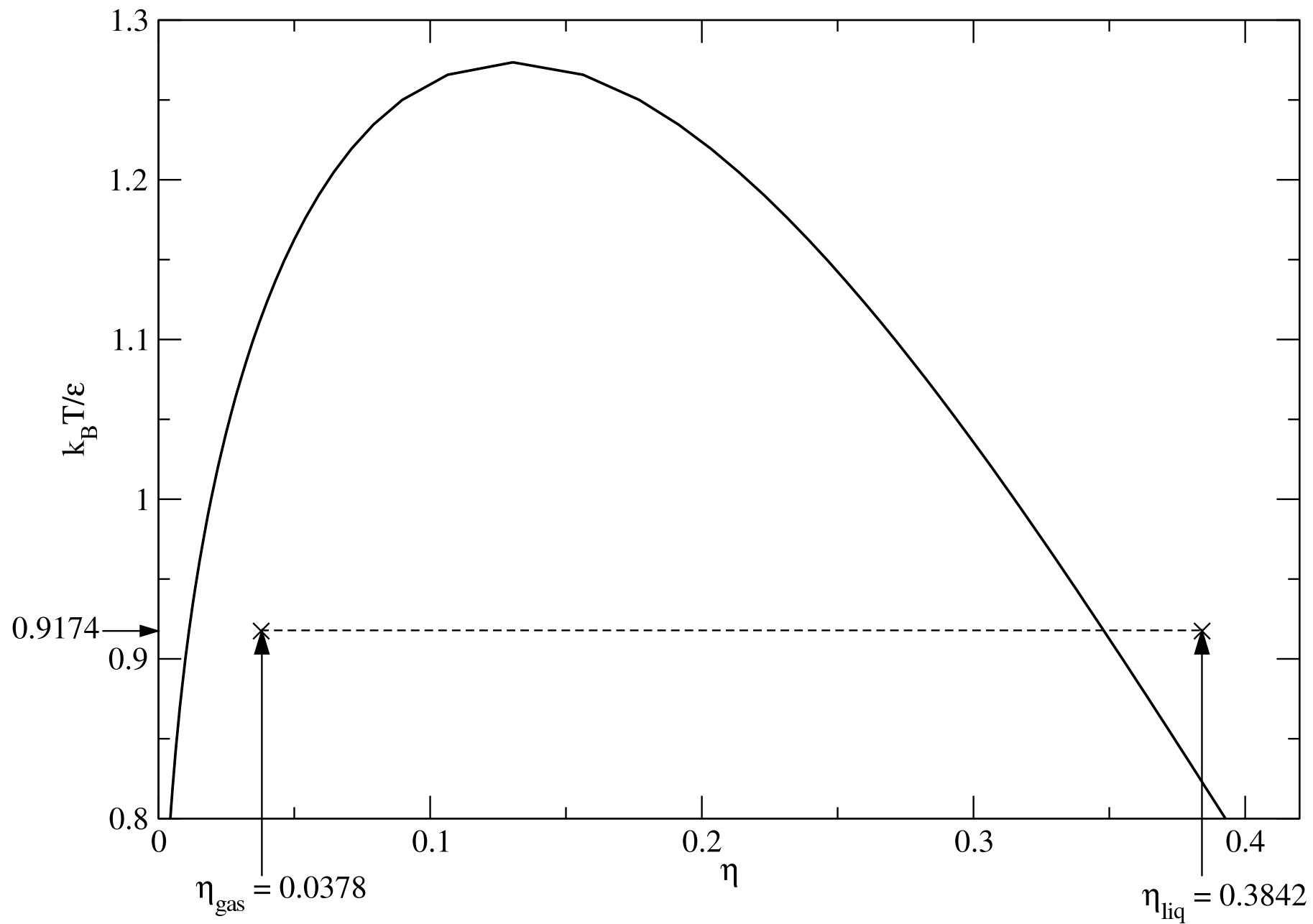
and the excess free energy density

$$\beta \Phi = -n_0 \ln(1 - n_3) + \frac{n_1 n_2 - \vec{n}_1 \cdot \vec{n}_2}{1 - n_3} + (n_2^3 - 3n_2 \vec{n}_2 \cdot \vec{n}_2) \frac{n_3 + (1 - n_3)^2 \ln(1 - n_3)}{36\pi n_3^2 (1 - n_3)^2}$$

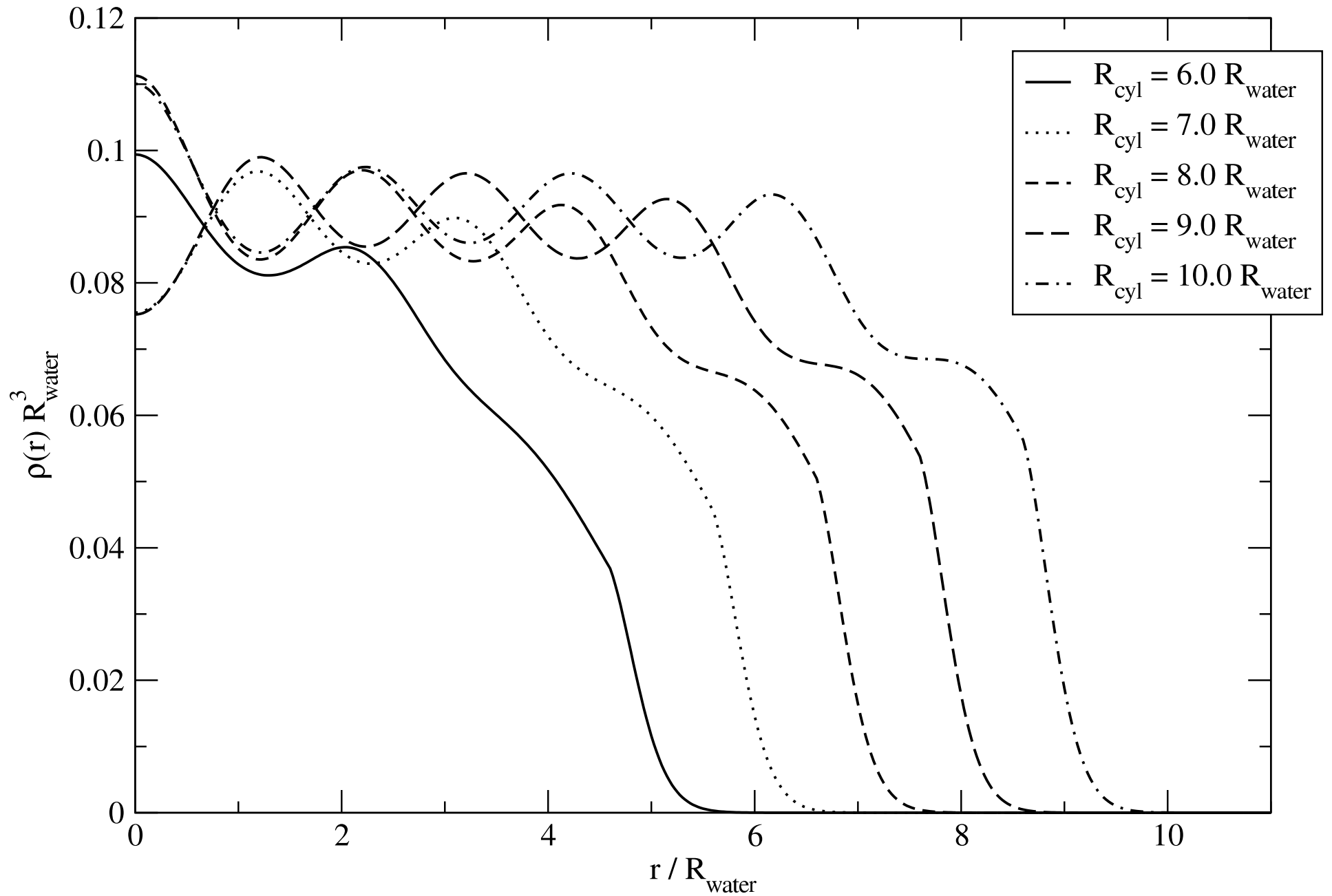
with weighted densities defined by

$$n_\alpha(\mathbf{r}) = \sum_{i=1}^{\nu} \int d^3r' \rho_i(\mathbf{r} - \mathbf{r}') \omega_\alpha^i(\mathbf{r}')$$

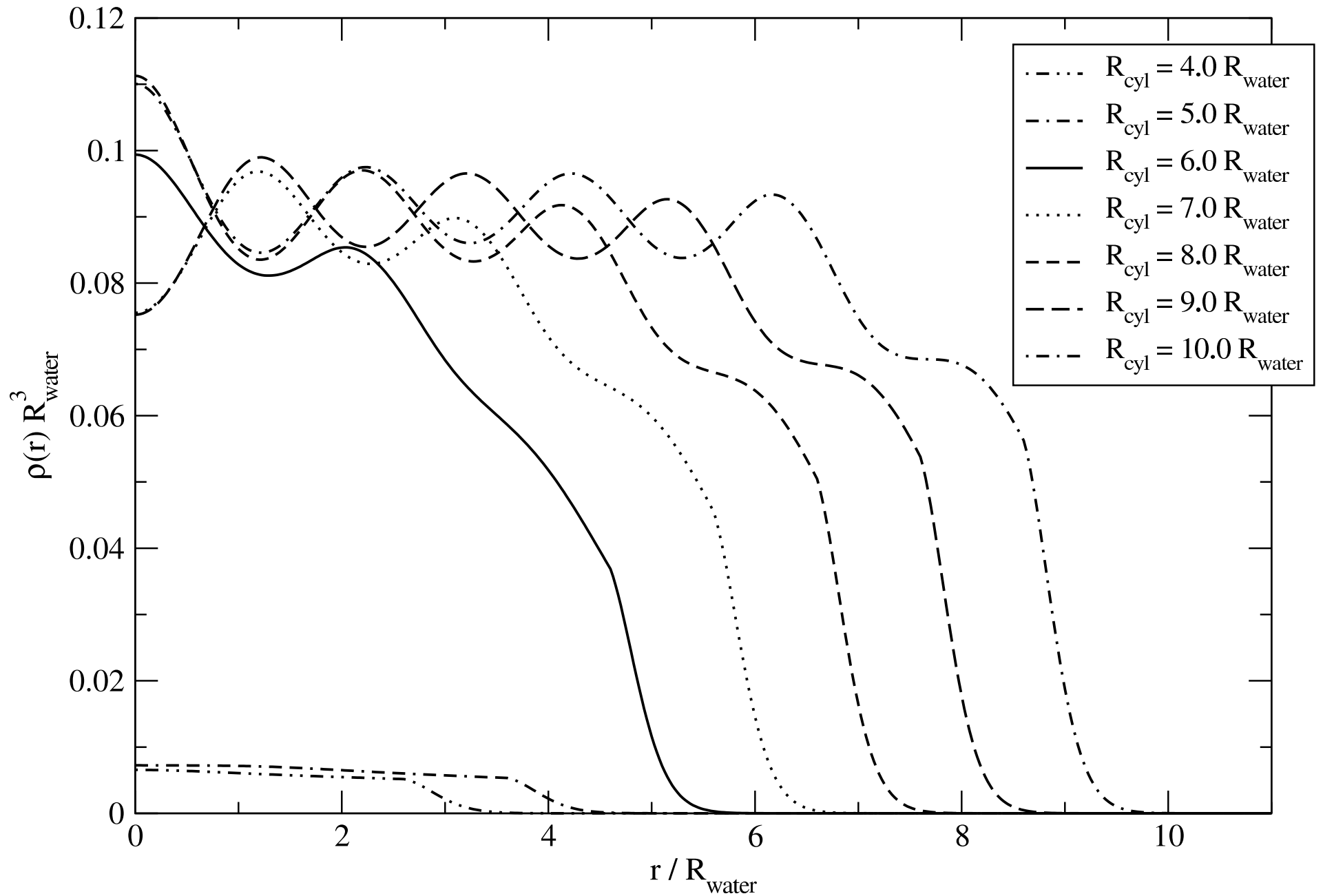
Phase Diagram



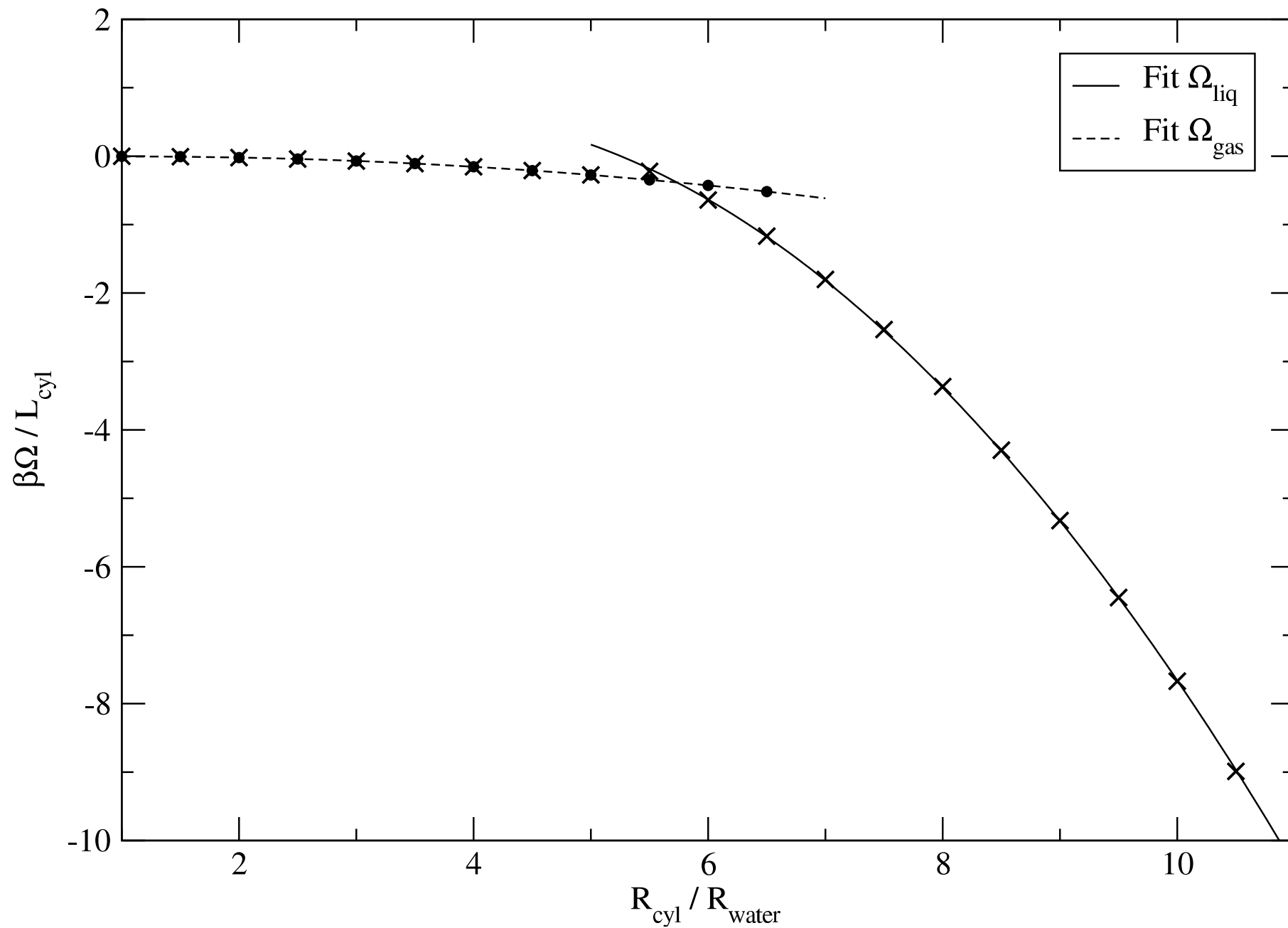
Density Profiles



Density Profiles



Capillary Evaporation



Thermodynamic Coefficients

- grand potential

$$\Omega_i(R_{cyl}) = -p_i V_{cyl}(R_{cyl}) + \sigma_i A_{cyl}(R_{cyl}) + \kappa_i C_{cyl}(R_{cyl})$$

$$V_{cyl} = \pi R_{cyl}^2 L_{cyl}, \quad A_{cyl} = 2\pi R_{cyl} L_{cyl}, \quad C_{cyl} = \pi L_{cyl}$$

– liquid side ($i = l$)

– gas side ($i = g$)

$$* \eta_l = \rho_l \frac{4\pi}{3} R_{water}^3 = 0.3841$$

$$* \eta_g = \rho_g \frac{4\pi}{3} R_{water}^3 = 0.0378$$

$$* \beta p_l R_{water}^3 = 6.077 \times 10^{-2}$$

$$* \beta p_g R_{water}^3 = 5.507 \times 10^{-3}$$

$$* \beta \sigma_l R_{water}^2 = 2.066 \times 10^{-1}$$

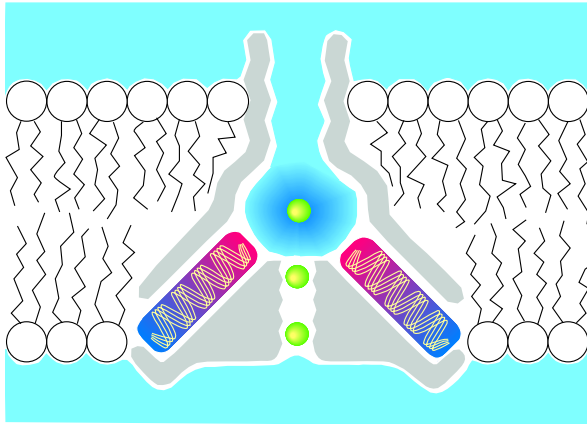
$$* \beta \sigma_g R_{water}^2 = 5.816 \times 10^{-3}$$

$$* \beta \kappa_l R_{water} = -4.93 \times 10^{-1}$$

$$* \beta \kappa_g R_{water} = -7.71 \times 10^{-3}$$

- liquid-gas surface tension: $\beta \sigma_{lg} R_{water}^2 = 8.549 \times 10^{-2}$

Geometry of a Channel



D.A. Doyle et al., Science **280**, 69 (1998).

- volume V
- surface area A
- local radii of curvature R_1 and R_2
 - integrated (over surface area) mean curvature

$$C = \frac{1}{4\pi} \int_{\partial V} H dS, \quad H = \frac{1}{2} \left(\frac{1}{R_1} + \frac{1}{R_2} \right)$$

- integrated (over surface area) Gaussian curvature

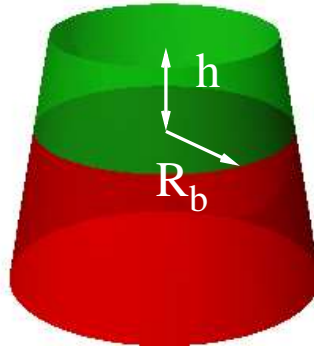
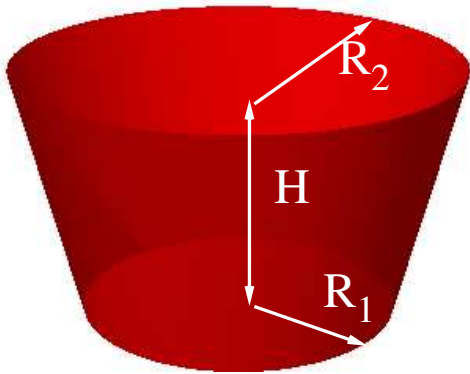
$$X = \frac{1}{4\pi} \int_{\partial V} K dS, \quad K = \frac{1}{R_1} \frac{1}{R_2}$$

- morphometric ansatz for grand potential

$$\Omega = -pV + \sigma A + \kappa C + \bar{\kappa} X$$

P.-M. König, R. Roth and K.R. Mecke, Phys. Rev. Lett. **93**, 160601 (2004).

Model Geometry of the Gate



- $H = 18\text{\AA}$ (fixed)
- $R_1 = 9\text{\AA}$ (fixed)
- R_2 can vary
- h must be calculated

- open gate

$$\Omega_{gate}^{op} = -p_l V(H, R_1, R_2) + \sigma_l M(H, R_1, R_2) + \kappa_l C(H, R_1, R_2)$$

- closed gate

$$\begin{aligned}\Omega_{gate}^{cl} = & -p_l V(H - h, R_1, R_b) + \sigma_l M(H - h, R_1, R_b) + \kappa_l C(H - h, R_1, R_b) \\ & -p_g V(h, R_b, R_2) + \sigma_g M(h, R_b, R_2) + \kappa_g C(h, R_b, R_2) \\ & + \sigma_{gl} (A(R_b) + A(R_2))\end{aligned}$$

Geometrical Measures

- volume

$$V(h, R_1, R_2) = \frac{\pi h}{3} (R_1^2 + R_2^2 + R_1 R_2)$$

- surface (cone shell)

$$M(h, R_1, R_2) = \pi(R_1 + R_2)\sqrt{h^2 + (R_1 - R_2)^2}$$

- integrate mean curvature

$$C(h, R_1, R_2) = \pi h$$

- area of liquid-gas interface

$$A(R) = \pi(R - R_{water})^2$$

Thermodynamics

- for $R_2 < R_2^{max}$

$$\Omega_{gate}^{cl}(h, R_2) - \Omega_{gate}^{op}(R_2) < 0$$

- bubble height h_0 from

$$\left. \frac{\partial}{\partial h} \left(\Omega_{gate}^{cl}(h, R_2) - \Omega_{gate}^{op}(R_2) \right) \right|_{h=h_0} = 0$$

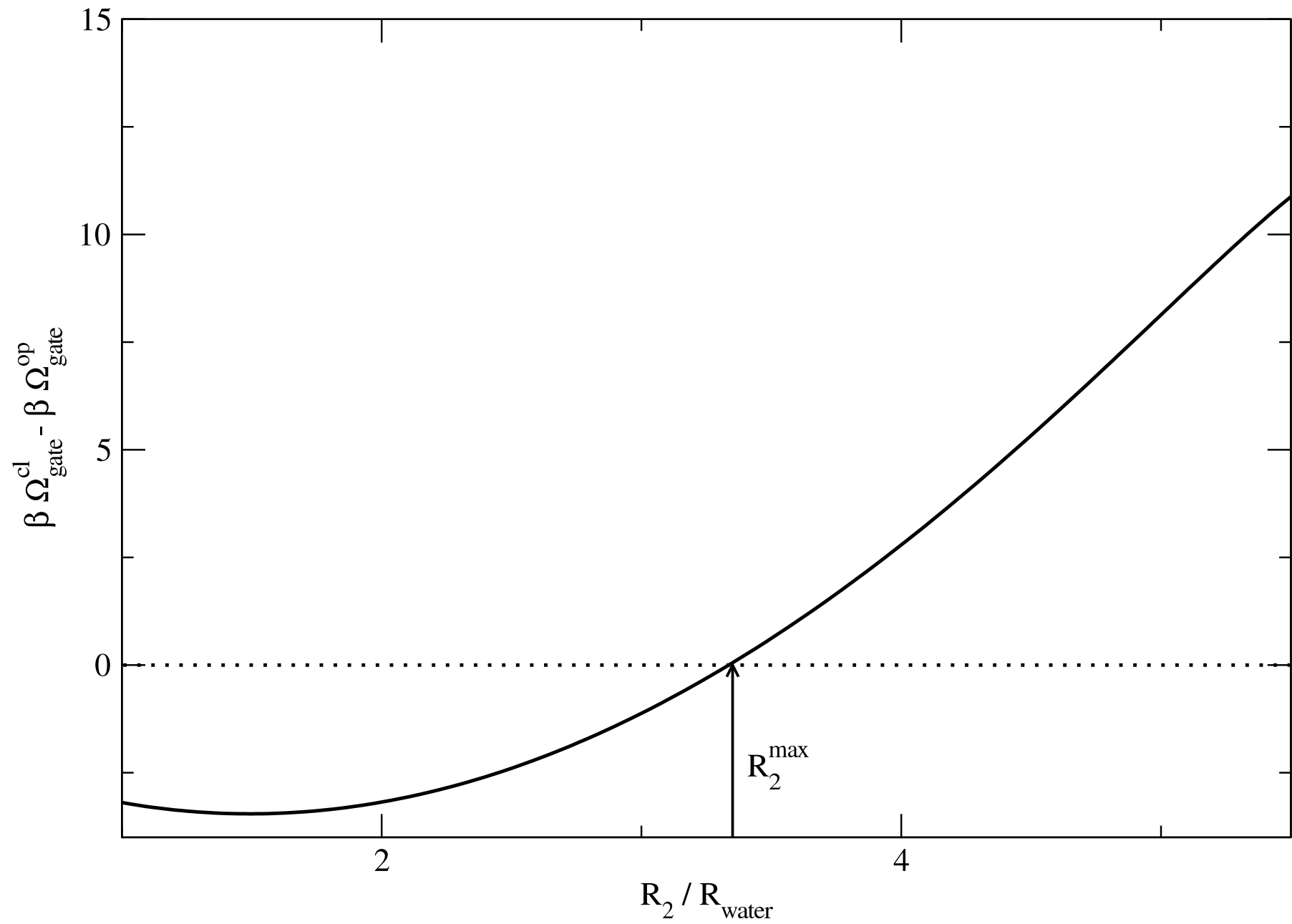
- required energy: R_2 changes from $R_2^{op} > R_2^{max}$ to $R_2^{cl} < R_2^{max}$

$$\Delta\Omega = \Omega_{gate}^{cl}(h(R_2^{cl}), R_2^{cl}) - \Omega_{gate}^{op}(R_2^{op})$$

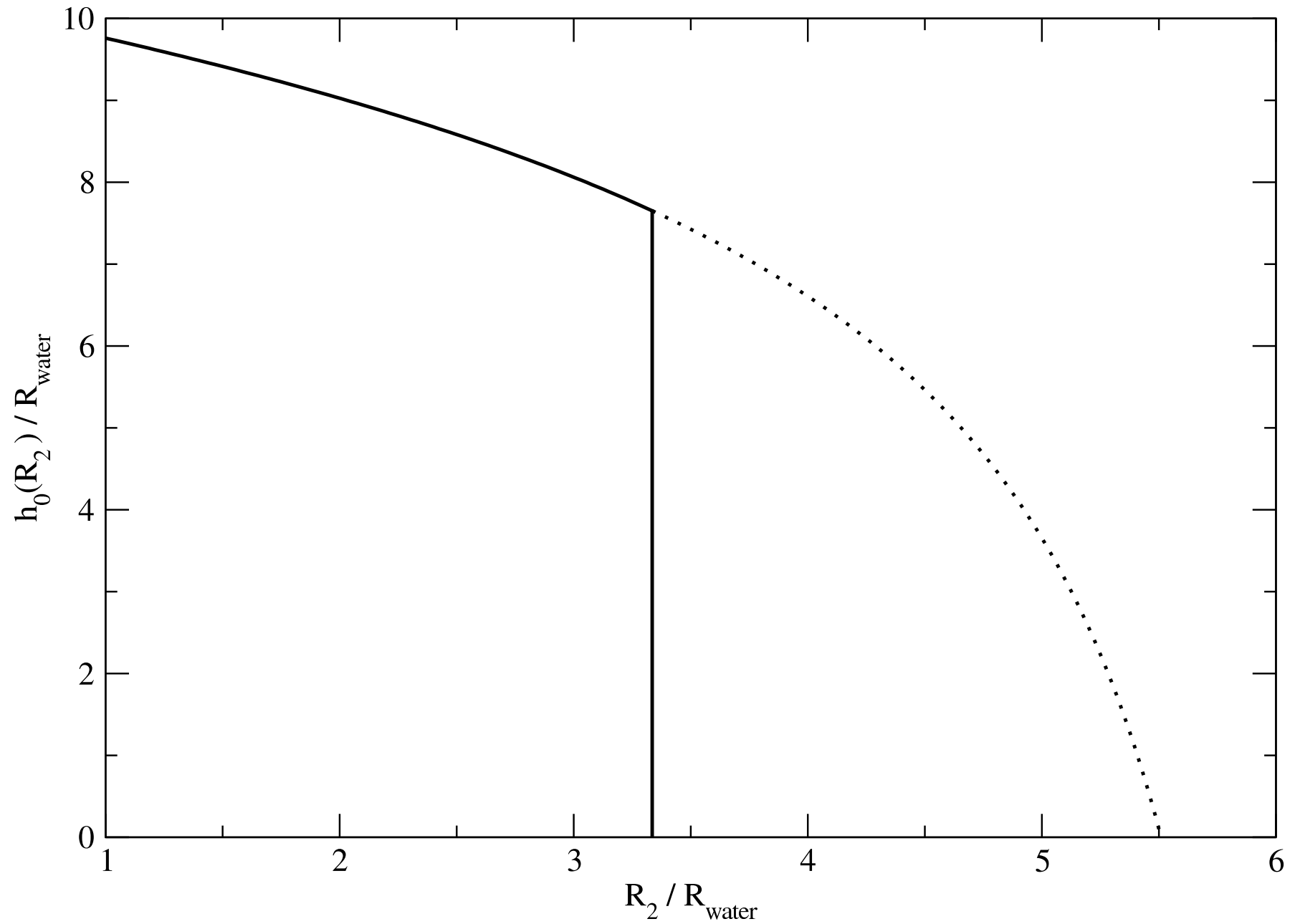
- force on protein

$$F(R_2) = -\frac{\partial}{\partial R_2} \Omega_{gate}(R_2)$$

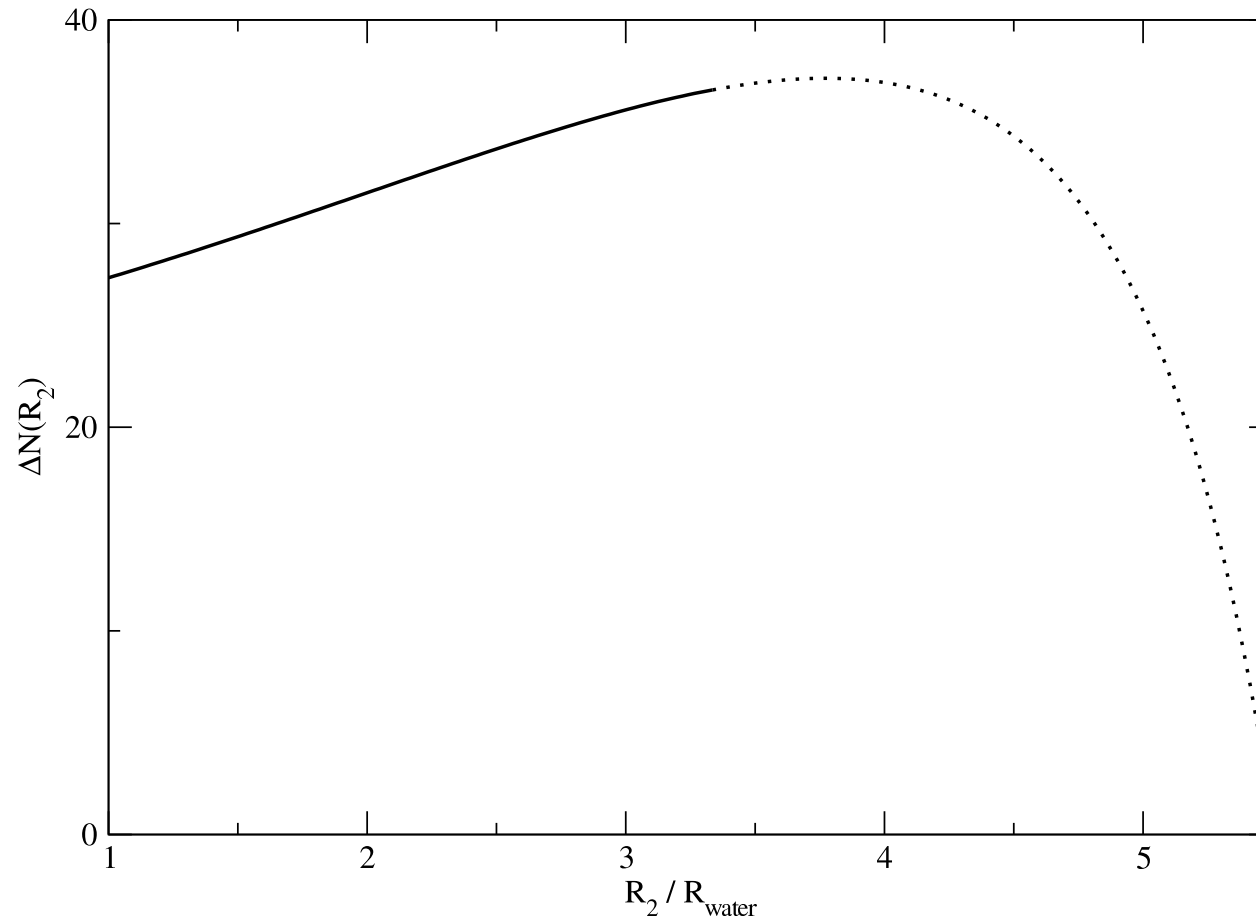
Stability of the Bubble



Bubble Height $h_0(R_2)$

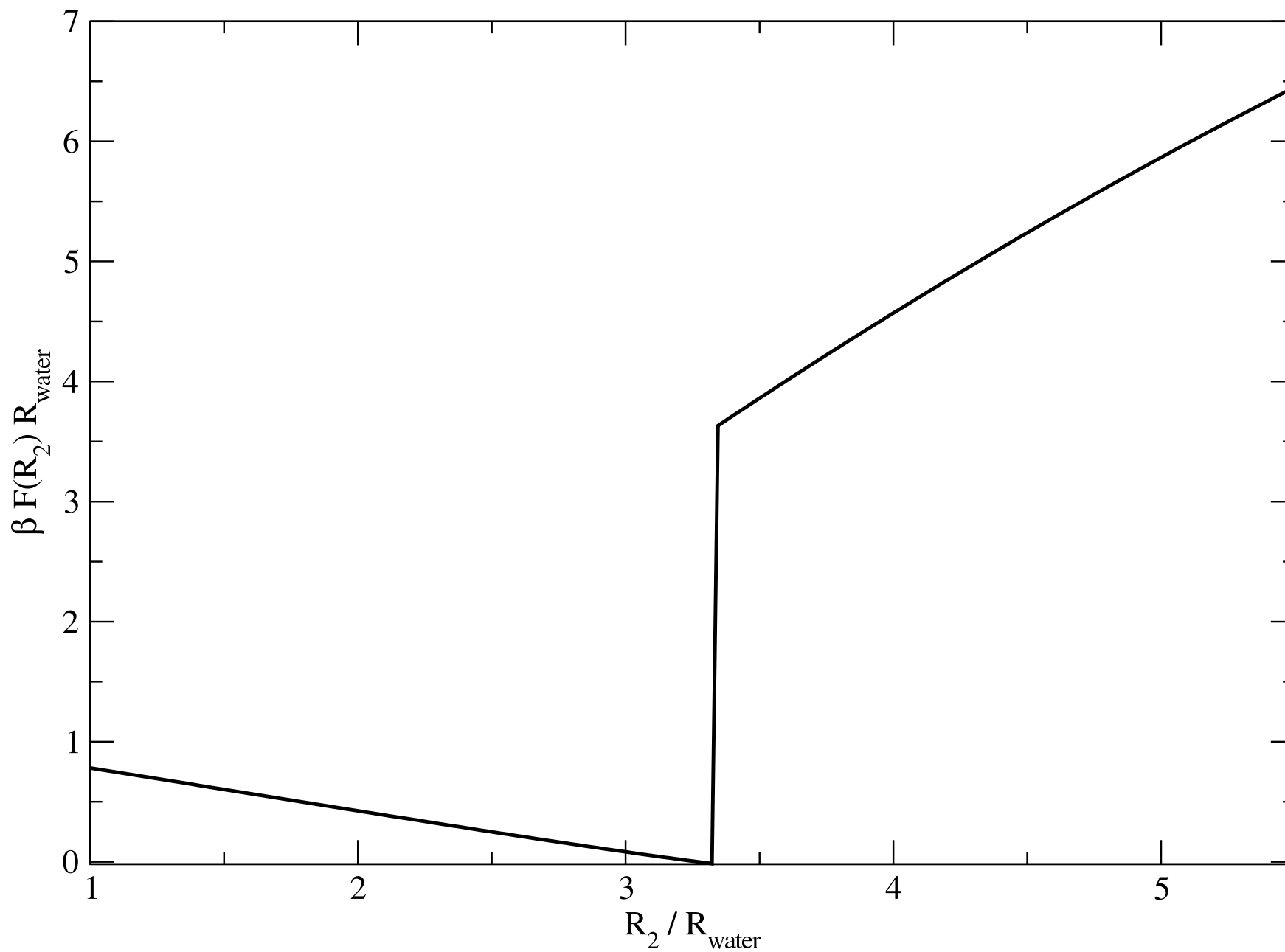


How much Water evaporates?



$$\Delta N(R_2) = (\rho_l - \rho_g)V(h, R_2, R_b)$$

Force on Protein



Required Energy

- when gate is open: liquid should be stable
- when gate is closed: bubble should be stable
- if $\Omega_{gate}^{cl}(h, R_2) - \Omega_{gate}^{op}(R_2) \sim 0$: big fluctuations
- if changes in R_2 are too large then energy costs are too big
- $R_2^{cl} \approx R_2^{max} - 2 \text{ \AA}$, $R_2^{op} \approx R_2^{max} + 1.5 \text{ \AA}$

$$\Delta\Omega = \Omega_{gate}^{cl}(h(R_2^{cl}), R_2^{cl}) - \Omega_{gate}^{op}(R_2^{op}) \approx 5k_B T$$