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Conference: From DNA-Inspired Physics to Physics-Inspired Biology

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Amphiphile-DNA complexes: adsorption, delivery and release

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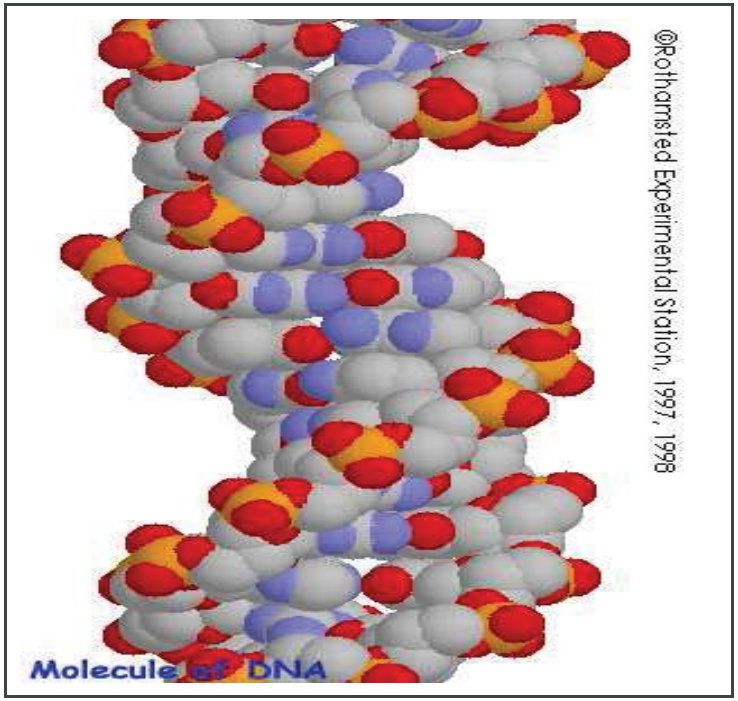
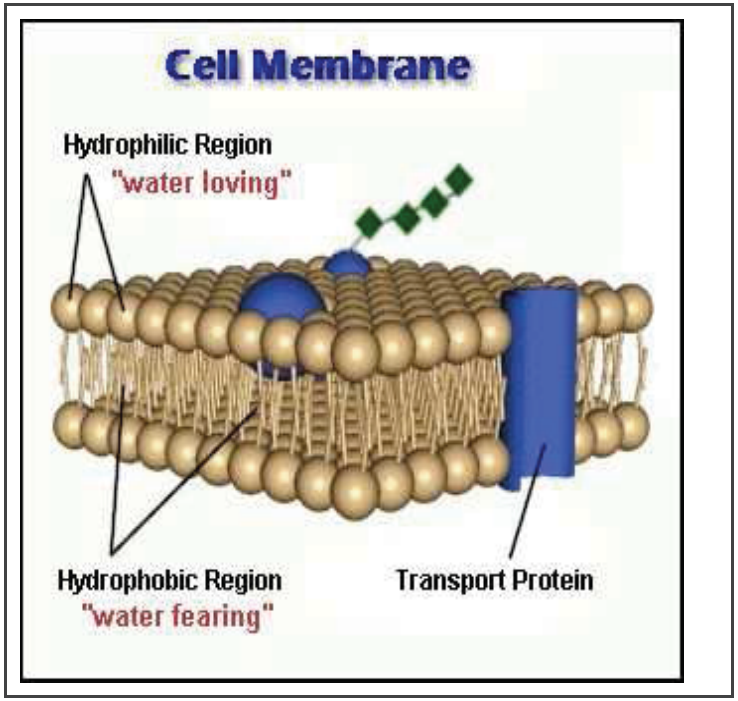
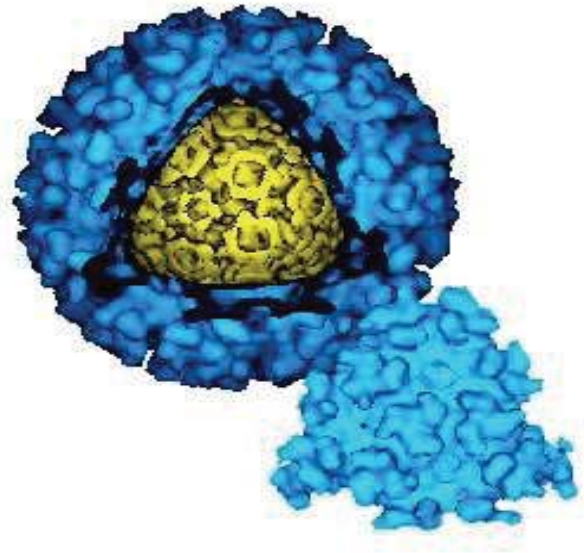
How to introduce DNA into a cell?





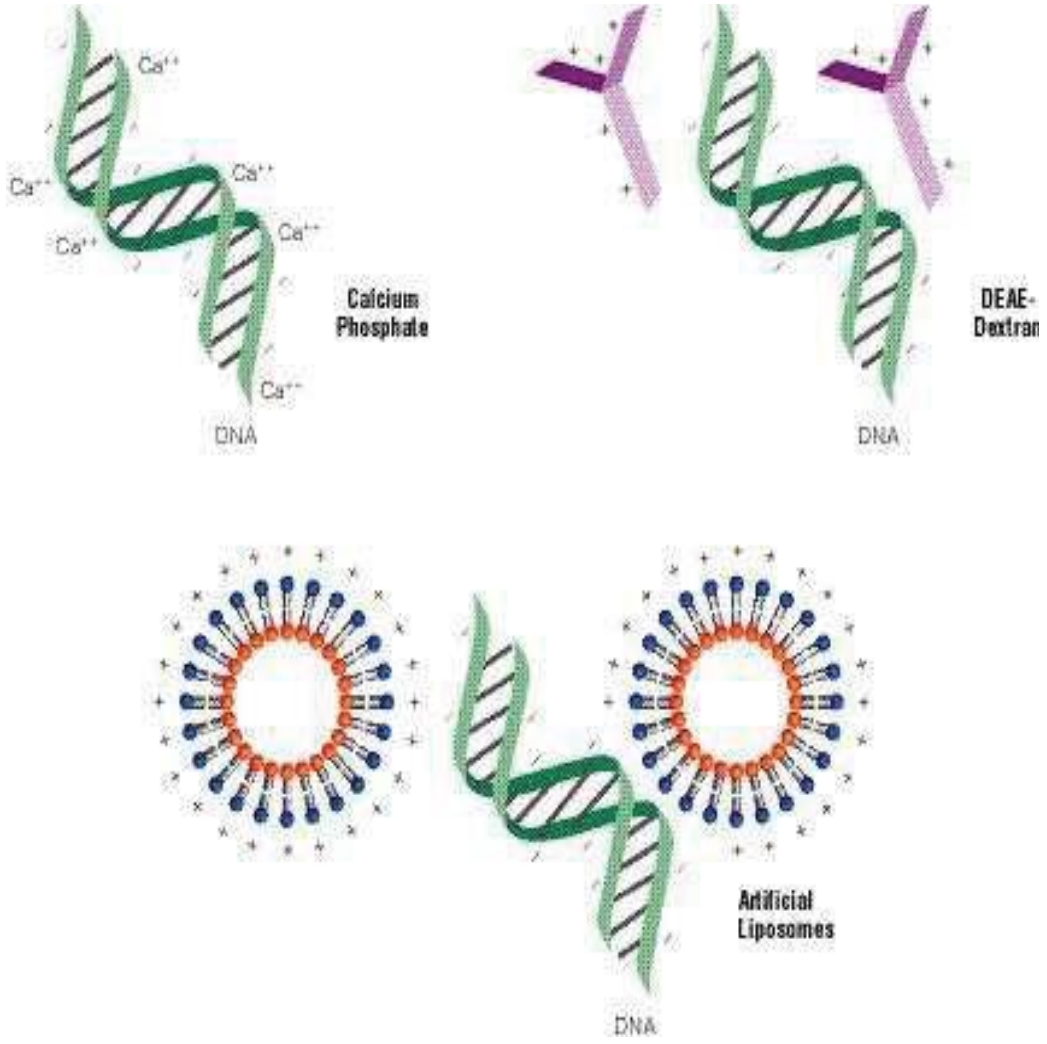
Usual Approach: Virus



Virus are DNA inside a shell.

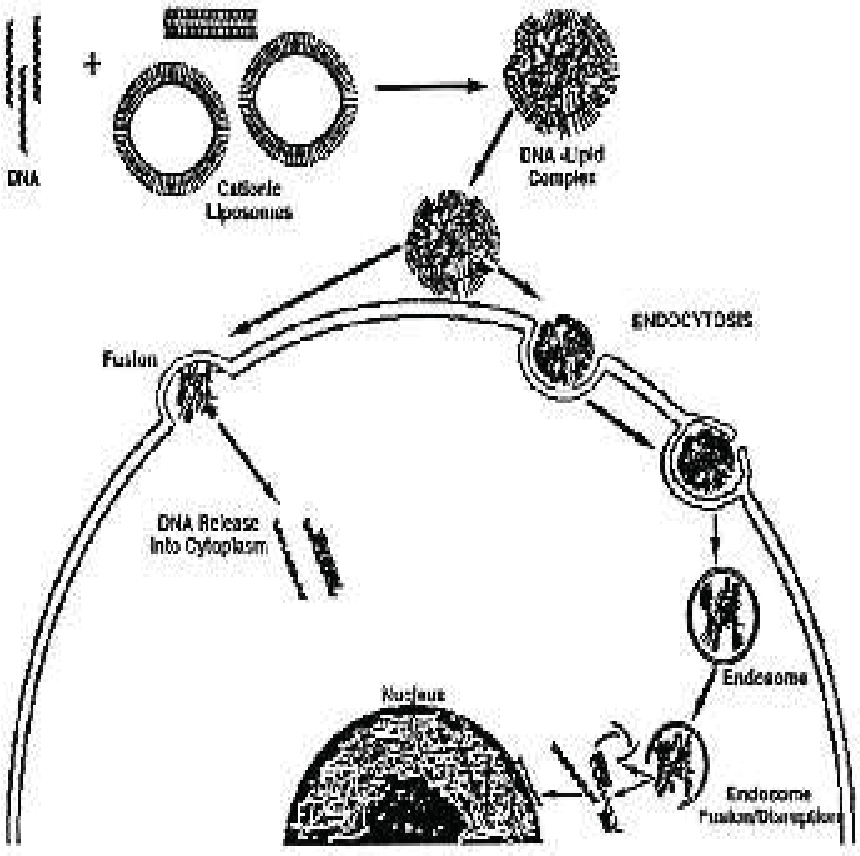
- Method: **Replace viral DNA inside the shell**
- Problem: **Left over viral DNA**

The Lipoplex: DNA + cationic lipids



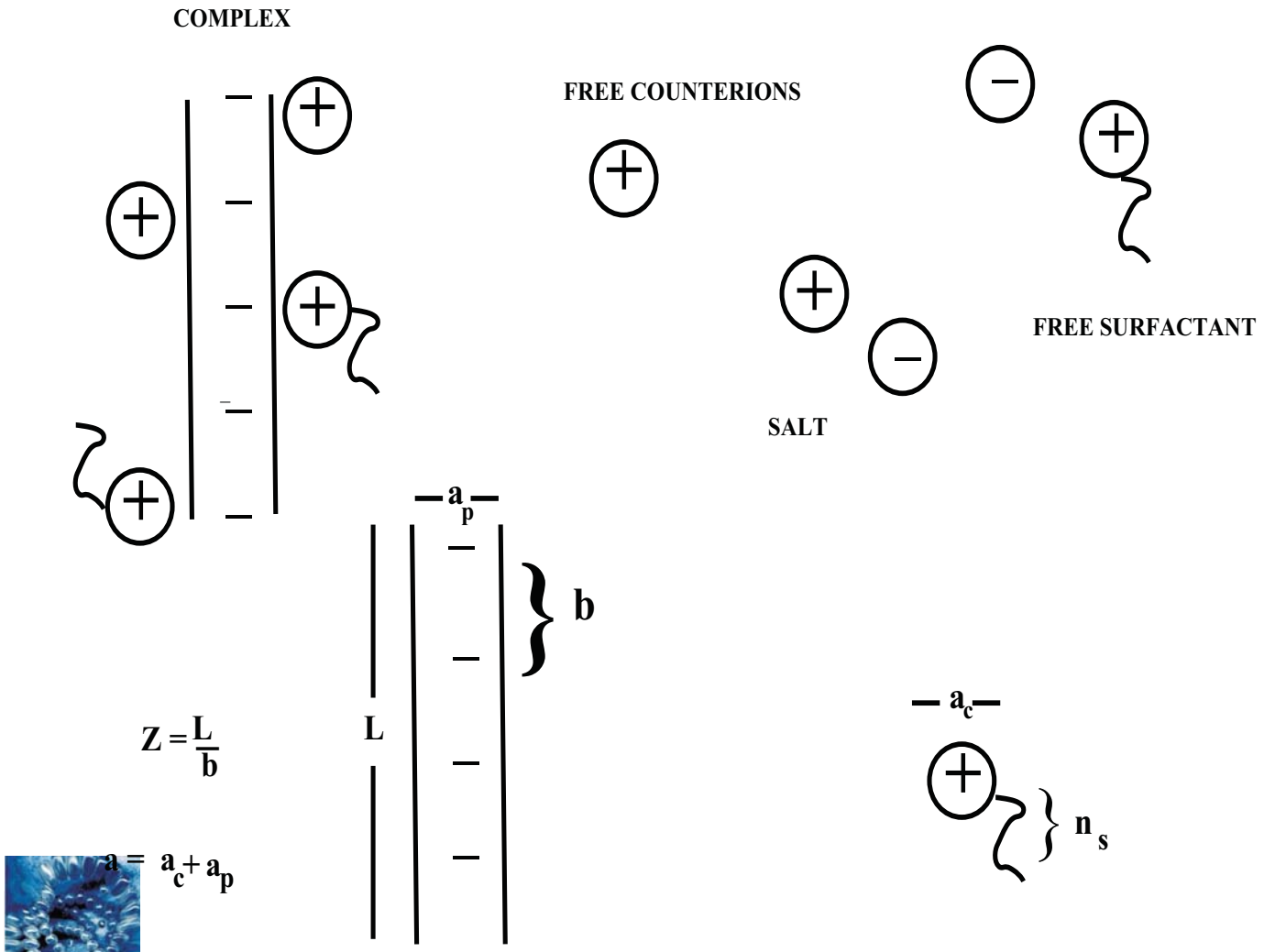
Idea: **DNA + lipossomes = positive complex**

The Transfection



Problem: **Cationic lipids are toxic!**

The Model


COMPLEX
FREE COUNTERIONS
FREE SURFACTANT
SALT
a_p
b
L
$Z = \frac{L}{b}$
$a = a_c + a_p$
a_c
n_s

Helmholtz Free Energy

$$F = F^{el} + F^{ent}$$

- Free energy as a function n_c and n_s
- Minimize free energy to find n_c and n_s.

The Entropic Free Energy

- Entropy of Free Surfactant

$$\beta f_s^{ent} = \left[\rho_s \ln \left(\frac{\phi_s}{z_s} \right) - \rho_s \right]$$

- Entropy of Complex

$$\beta f_p^{ent} = \left[\rho_p \ln \left(\frac{\phi_p (Z + n_c + n_s)}{(Z + z_s n_s + n_c)\zeta} \right) - \rho_p \right]$$

Internal Partion Function

$$H = \frac{q^2}{2} \sum_{i \neq j} \frac{[-1 + \sigma_c(i) + \sigma_s(i)][-1 + \sigma_c(i) + \sigma_s(j)]}{D[r(i) - r(j)]}$$

$$-\chi \sum_{i \neq j} \sigma_s(i)\sigma_s(j)$$

$$\ln \zeta = -\frac{\xi S}{Z}[n_c^2 + n_s^2 + 2n_c n_s - 2n_c - 2n_s] - \beta\chi n_s^2 \frac{Z-1}{Z^2}$$

$$-(1 - n_c - n_s)\ln[1 - n_c - n_s] + n_c \ln n_c + n_s \ln n_s$$

with $\xi = \beta q^2/(Db)$ and $S = Z[\Psi(Z) - \Psi(1)] - Z + 1$.

The Electrostatic Free Energy

$$\nabla^2\Psi(r) = -\frac{4\pi\rho_q(r)}{D}$$

$$\rho_q(r) = -\frac{\sigma_q\delta(r)}{2\pi r}$$

for $r < a$ and where $\sigma_q = -(Z - n_c - n_s)q/L$

$$\rho_q(r) = -(Z-n_c-n_s)q\rho_p+q\rho_+e^{-\beta q\Psi(r)}-q\rho_-e^{-\beta q\Psi(r)}+q\rho_s e^{-\beta q\Psi(r)}$$

for $r > a$

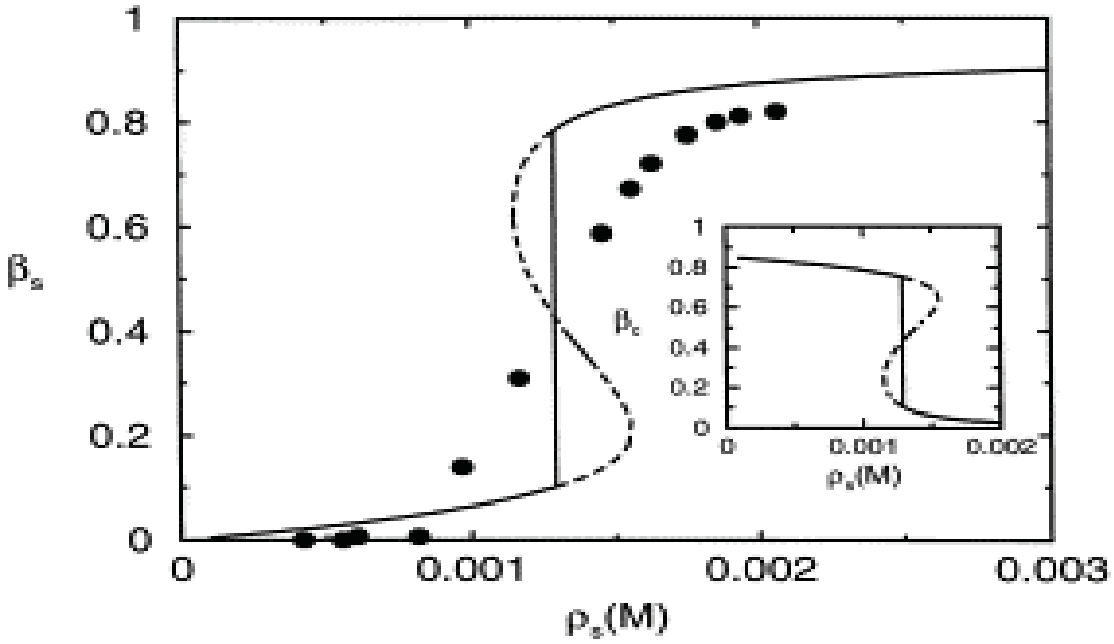
The Electrostatic Free Energy

$$U_{pc}^{el} = \frac{1}{2} \int \rho_q(r)[\Phi(r) - \Phi_{self}(r)]d^3r$$

$$F_{pc}^{el} = N_p \int_0^q \frac{2U^{el}(\bar{q})}{\bar{q}} d\bar{q}$$

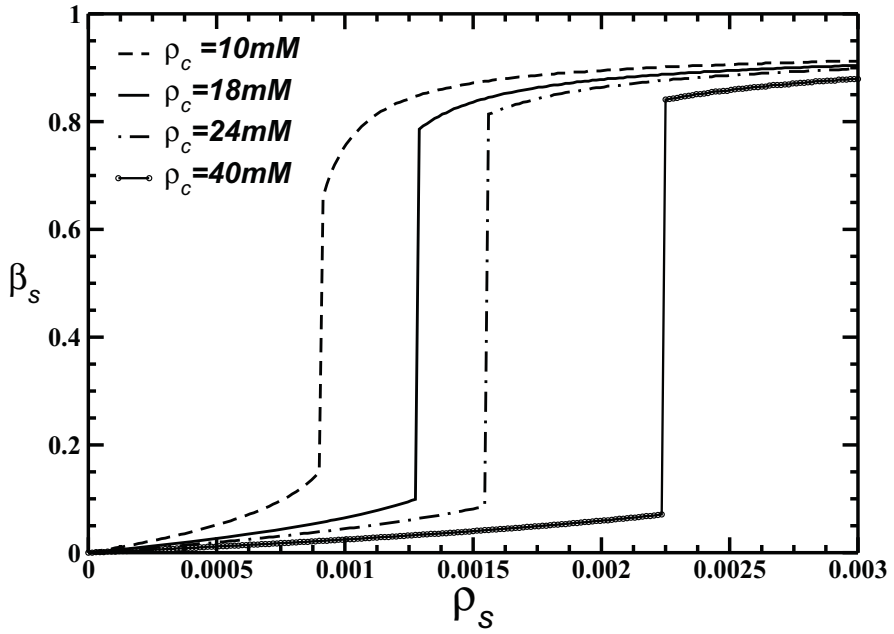
The Binding Isotherm

$$\chi = -3.5 k_B T, \rho_c = 18 mM,\ \rho_p = 2 \times 10^{-6} M, Z = 440$$



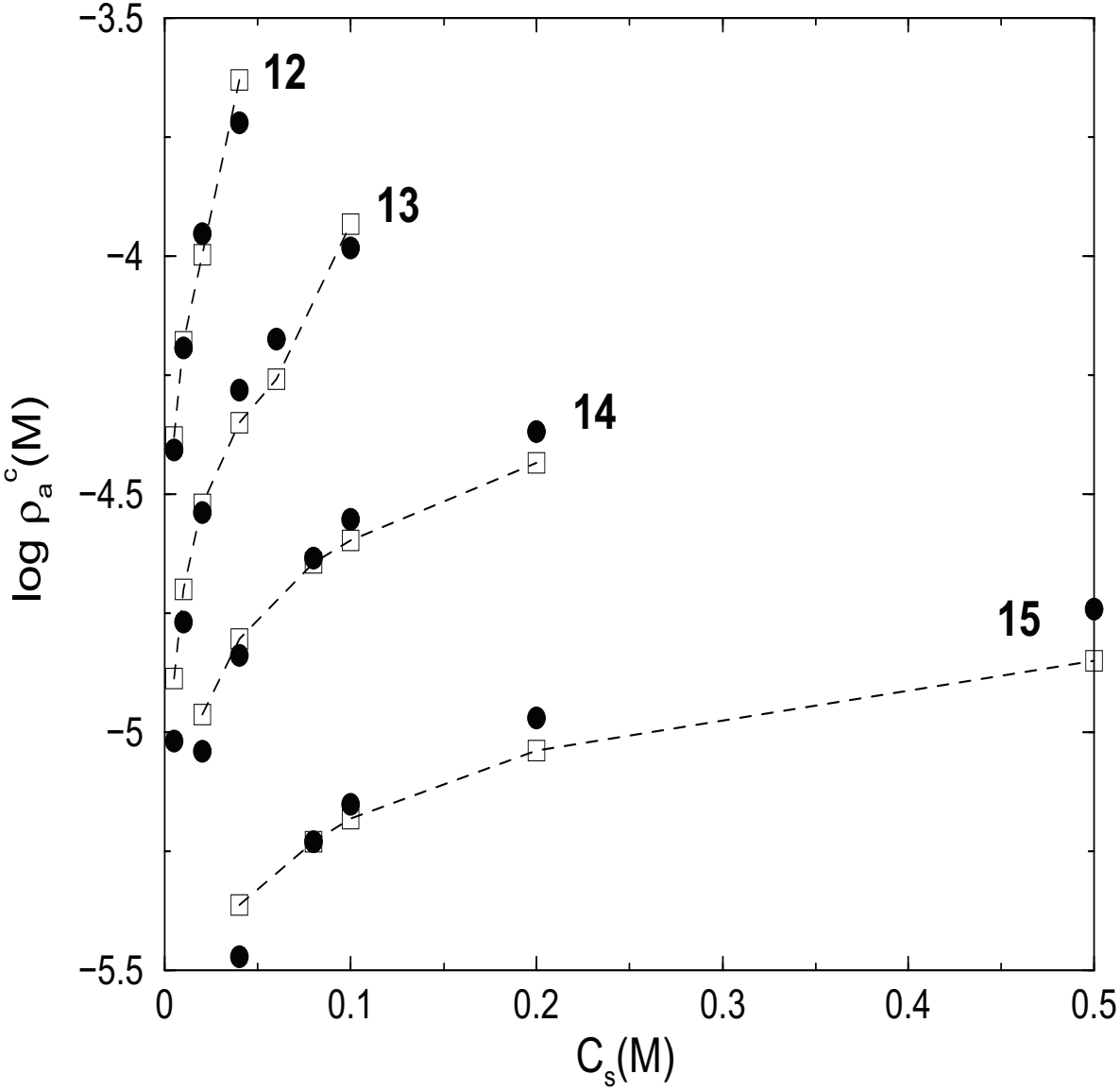
The Binding Isotherms

$$\chi = -3.5 k_B T \text{ and } \rho_p = 2 \times 10^{-6} M$$



Data: Gorelov *et al.* Physica A **249**, 216 (1998)

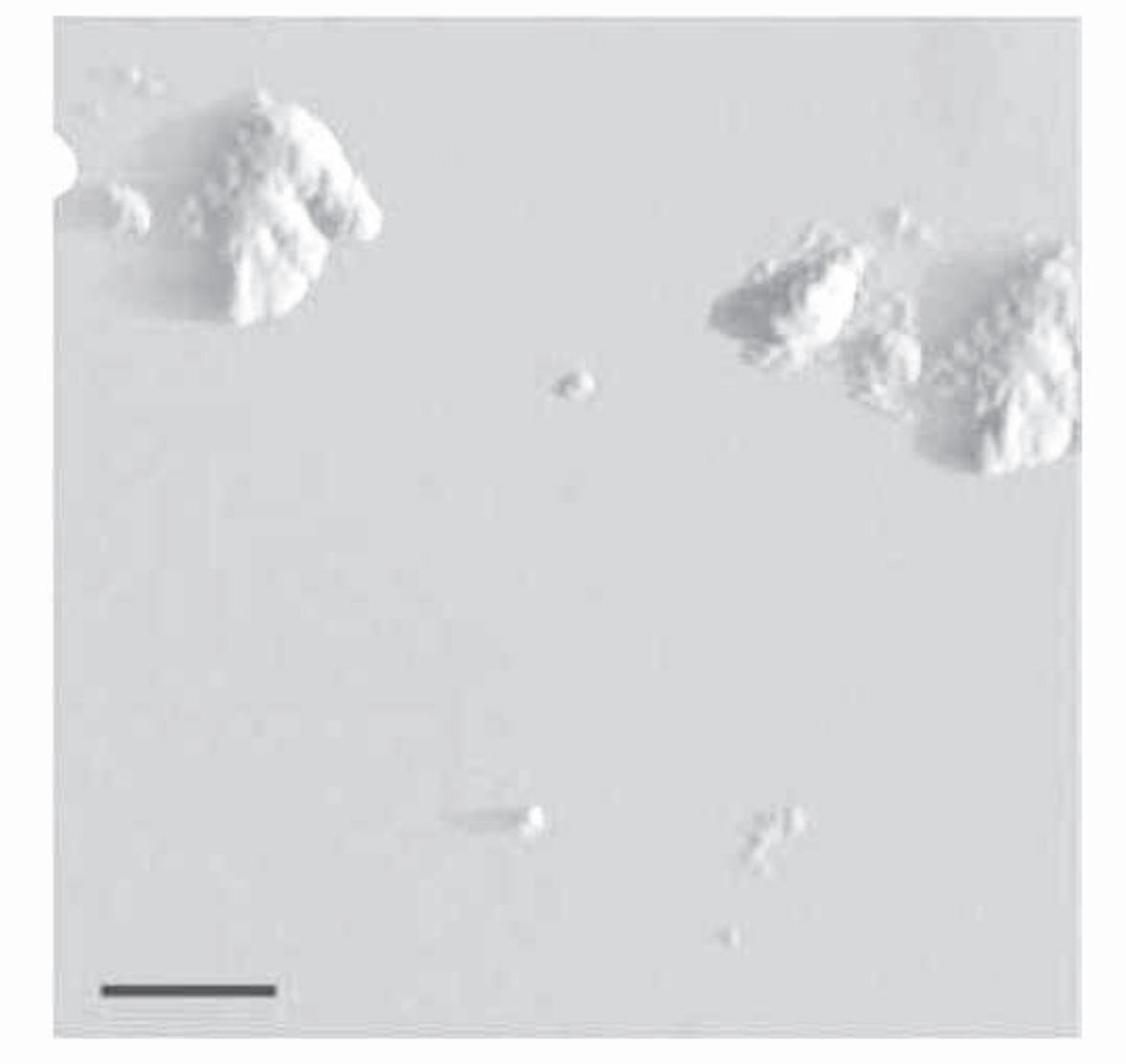
Sodium dextran sulfate



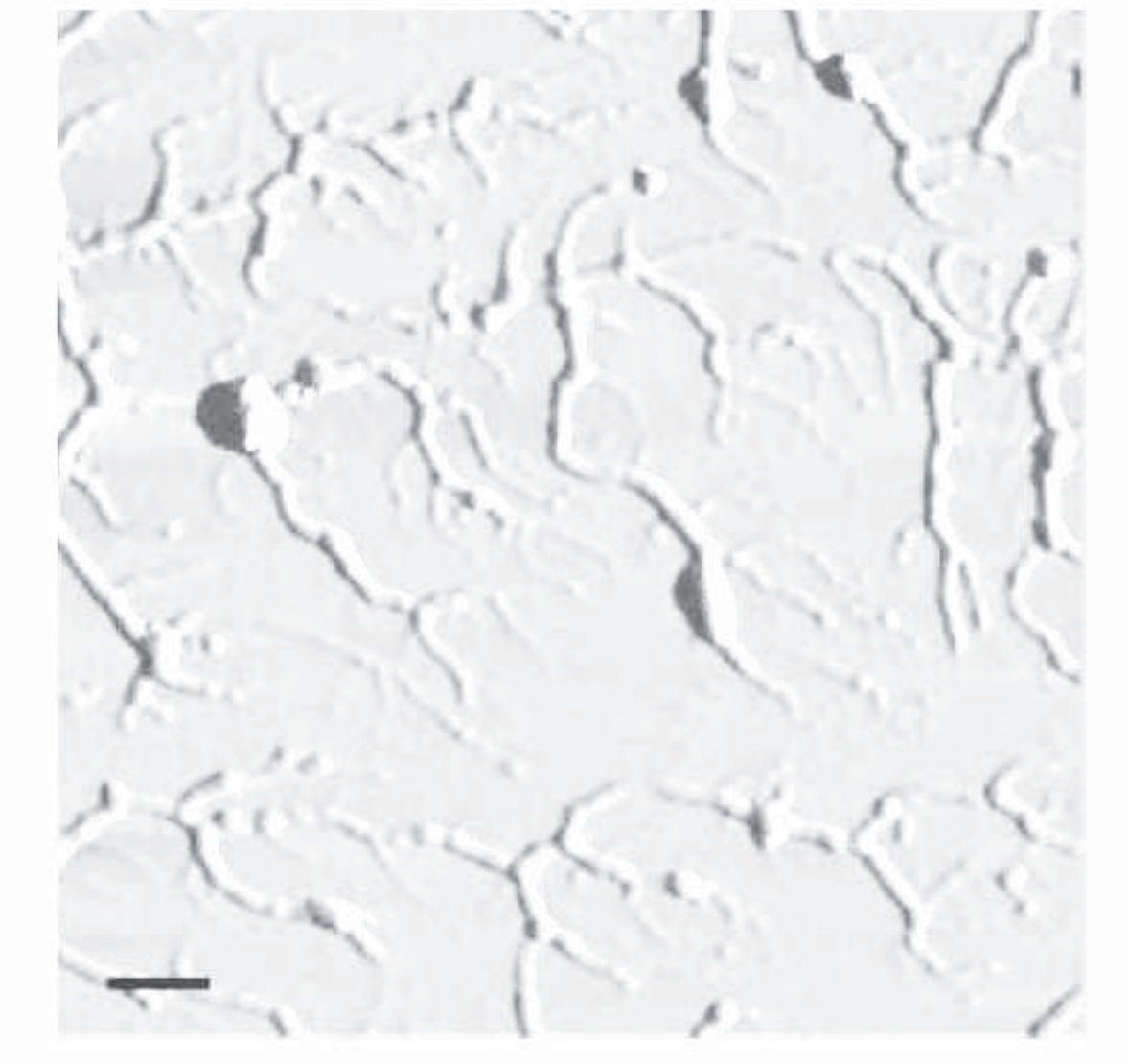
Transfection

- Plasmid pCH110 (7128bp) $\Rightarrow$ β-galactosidase enzyme
- Plasmid + Lipofectamine $\Rightarrow$ efficient transfection
- Linear DNA + Lipofectamine $\Rightarrow$ zero transfection
- Linear DNA more stable, better for vaxine
- Large concentration of Lipofectamine $\Rightarrow$ high toxicity
- New approach: minimal DNA + DDAB at CAC

Plasmid + Lipofectamine

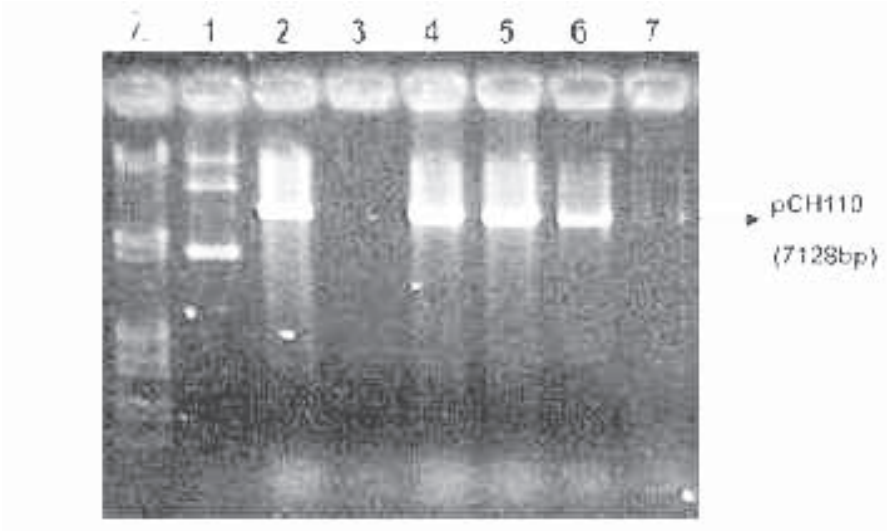


Linear DNA + Lipofectamine



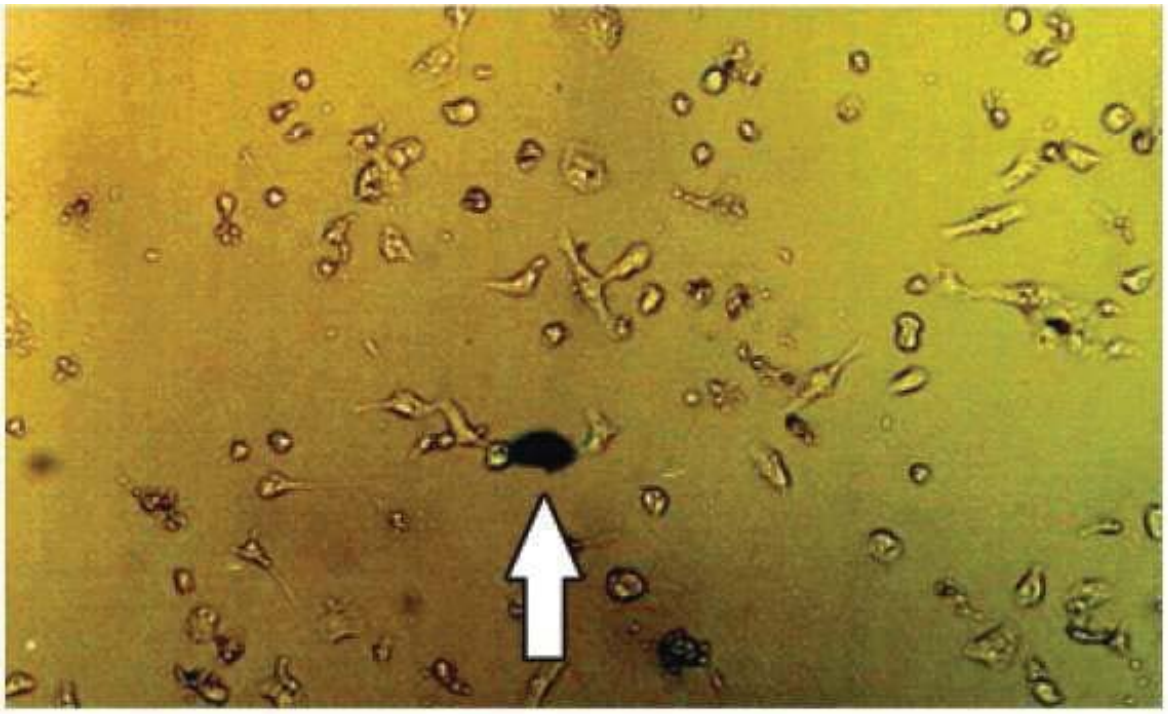
Gel electrophoresis

Staining by ethidium bromide → UV transillumination



- lane 1 → circular DNA
- lane 2 → linear DNA
- lane 3 → cicular DNA+Lipofectamine
- lane 4 → linear DNA+Lipofectamine (MRC)

Linear DNA+Lipofectamine $5\times$ MRC



Linear DNA+DDAB

Conclusions

- Association of minimal DNA-cationic lipid at CAC is a viable method for transfection.
- Lower transfection efficiency than plasmid+Lipofectamine.
- Need to understand the mechanism of transfection.