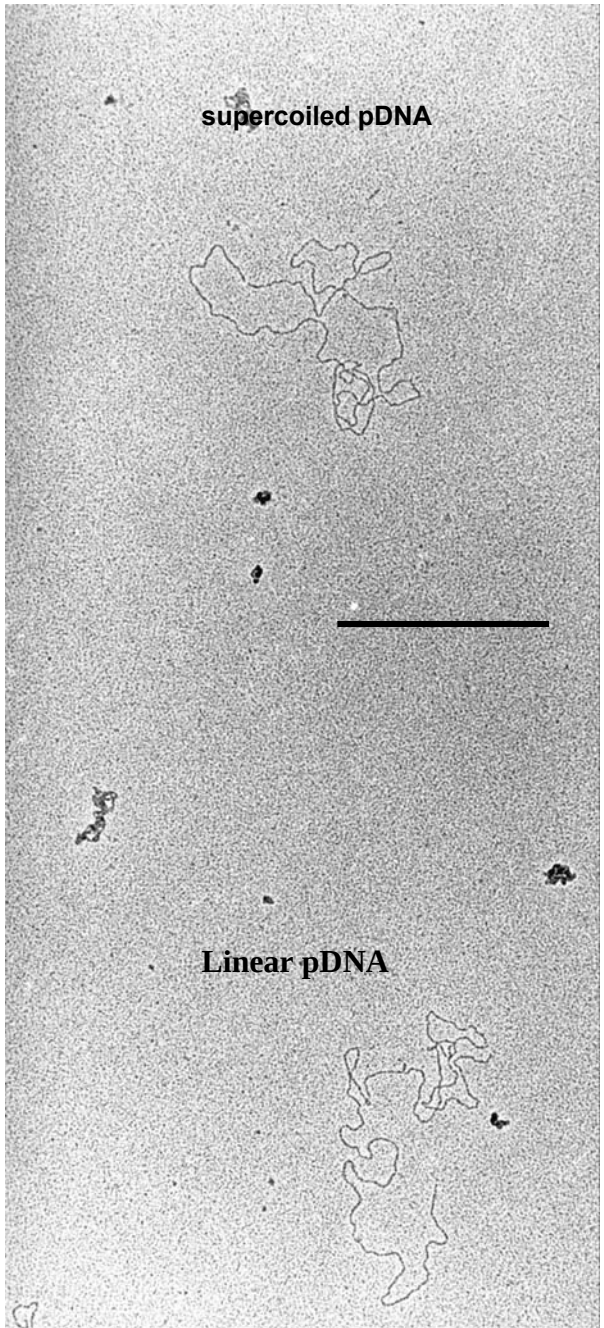
Ultrastructure of DLS and Neutraplex Lipoplexes



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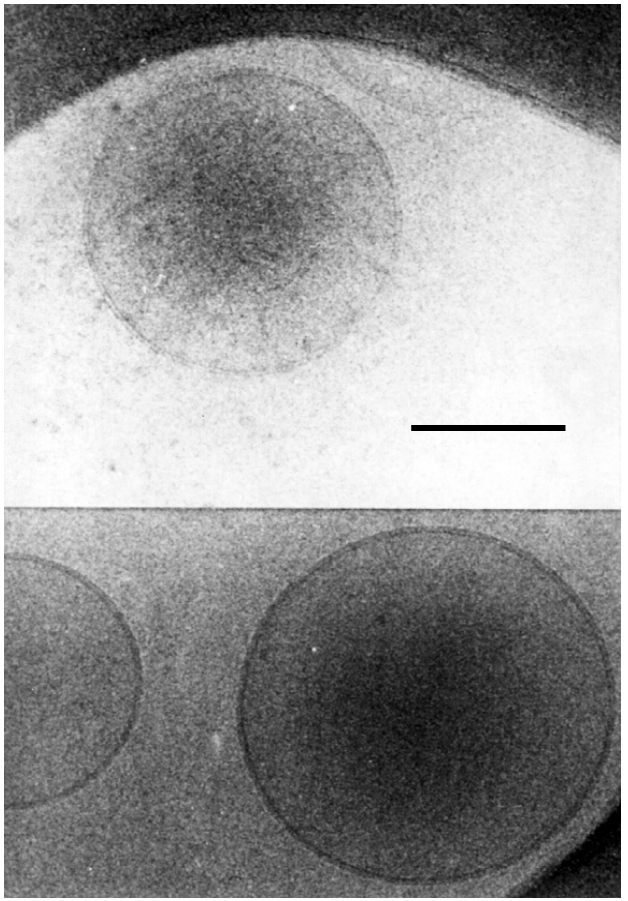

vesicles

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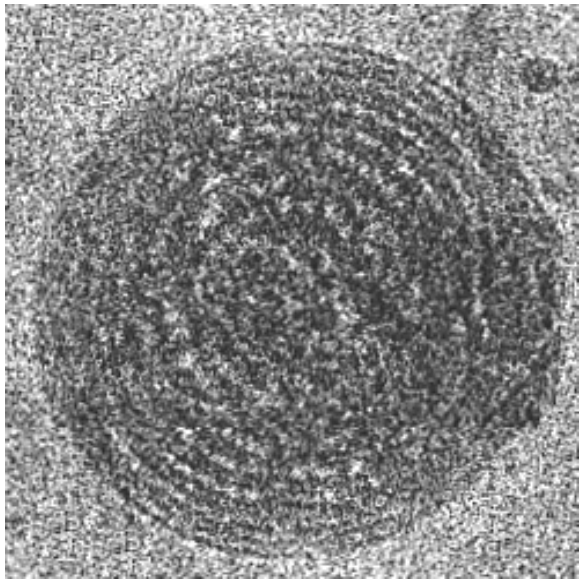


lipoplexes

Bar = 50 nm

(Thierry A.R. et al, BBA, 2009)

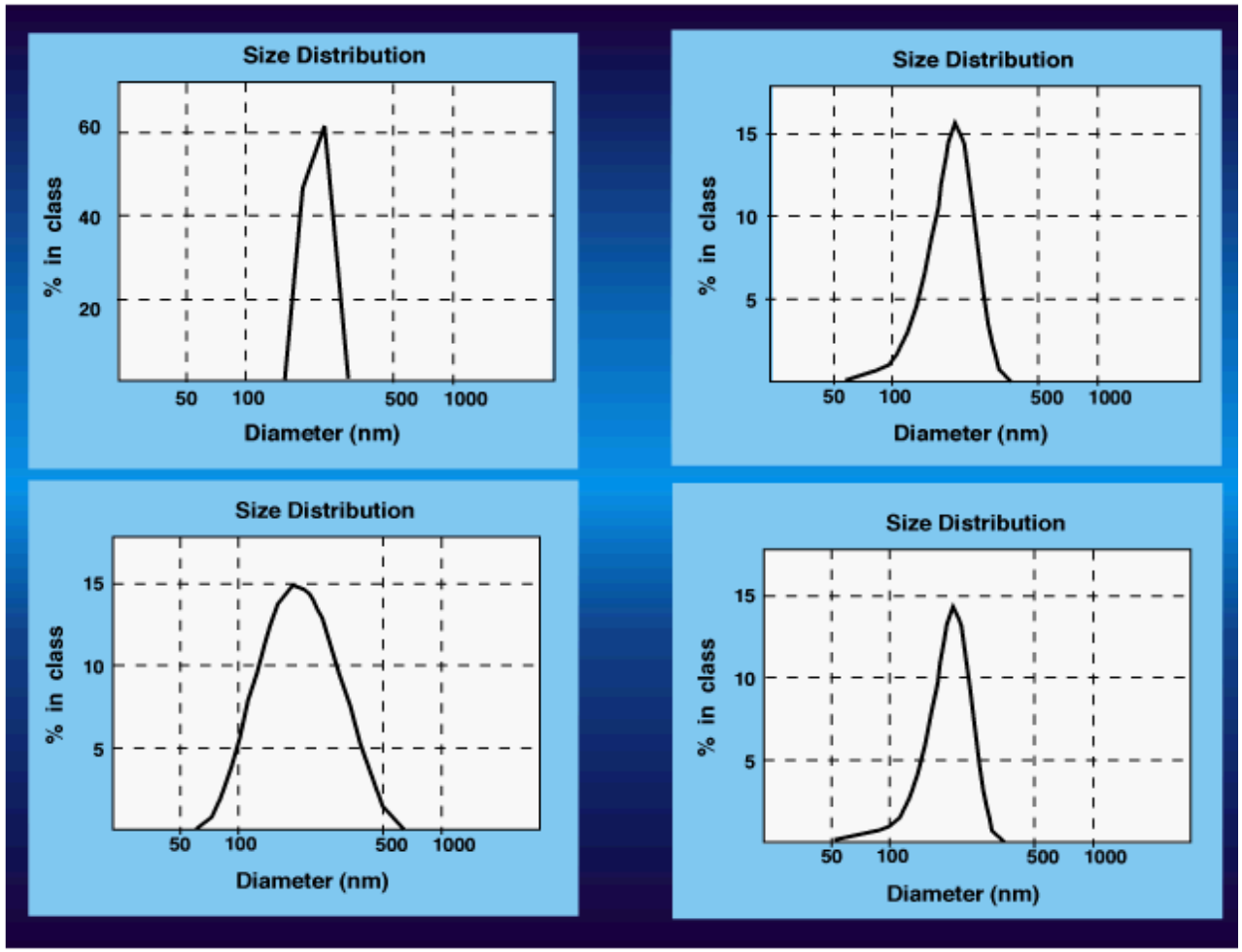
I. Ulstrastructure of Lipoplex

Distribution of particle size of Lipoplex formed with various types of DNA

Circular DNA

Plasmid
10 400 pb

254 nm
p = 0.193



Linear ds DNA

Replicative form
of M13 virus
7229 bp

221 nm
p=0.048

Linear ss DNA

M13 virus
7229 b

261 nm
p = 0.113

Oligodeoxynucléotides

synthetic
27 b

184 nm
p = 0.045

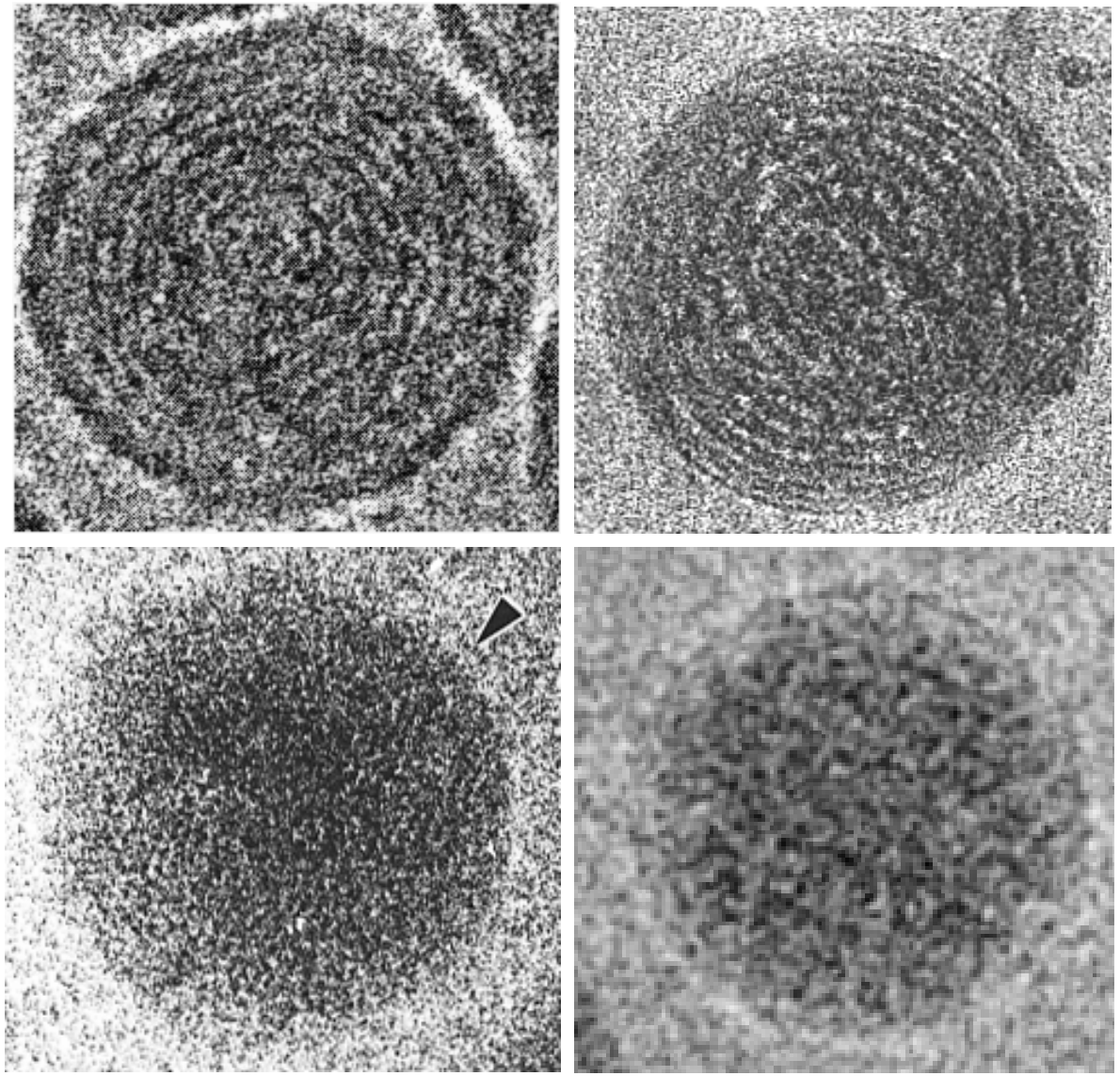
Dynamic Light Scattering

(Thierry A.R. et al, BBA, 2009)

I. Ulstrastructure of Lipoplex

Lipoplex are biomimetic nanostructures

Phage virus



Nx

(Thierry A.R. et al, BBA, 2009)

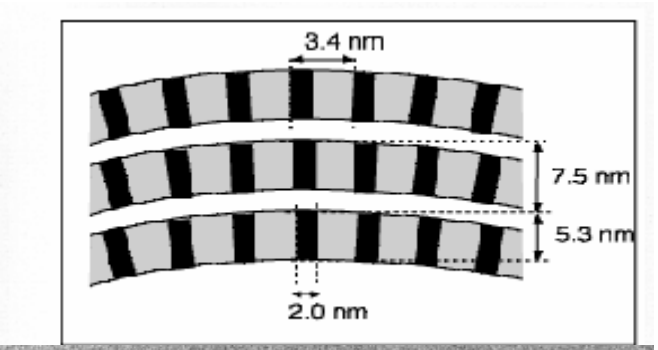
I. Ulstrastructure of Lipoplex

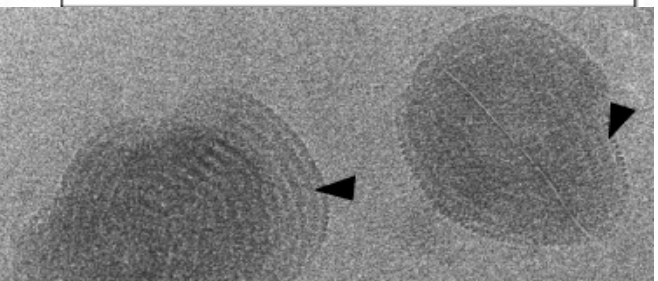
Phase transition of Lipoplex ultrastructures

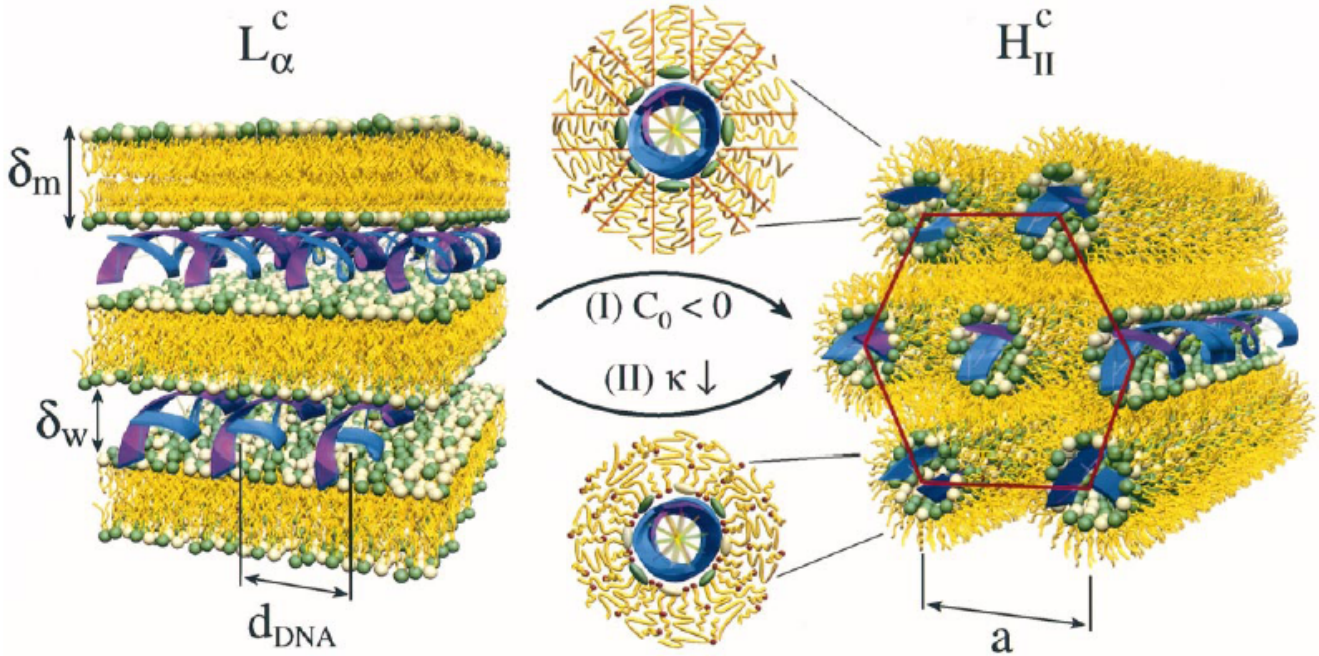
Does not fully explain:

- The 3D structure

- The transversal striation as observed by cryo-TEM





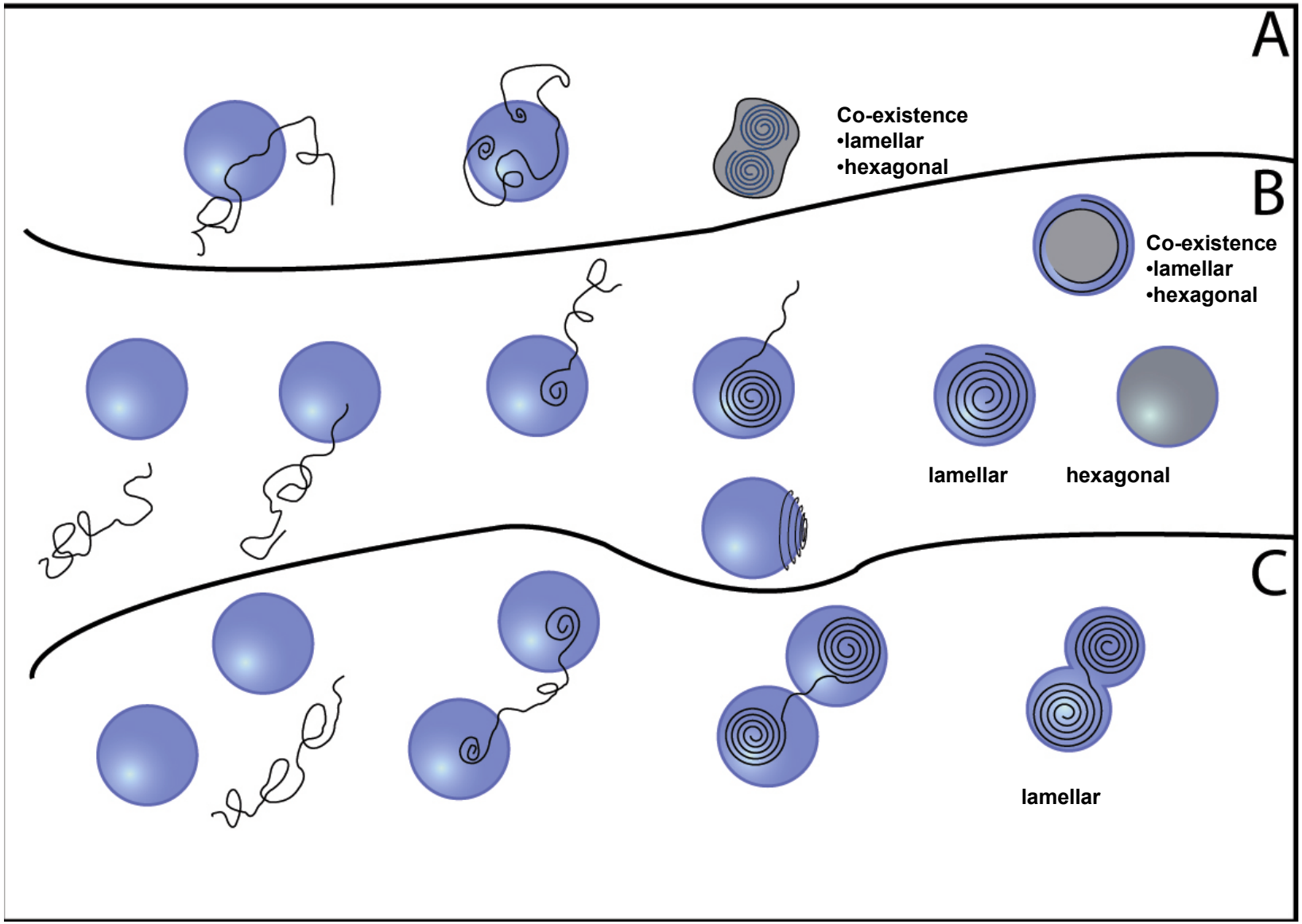


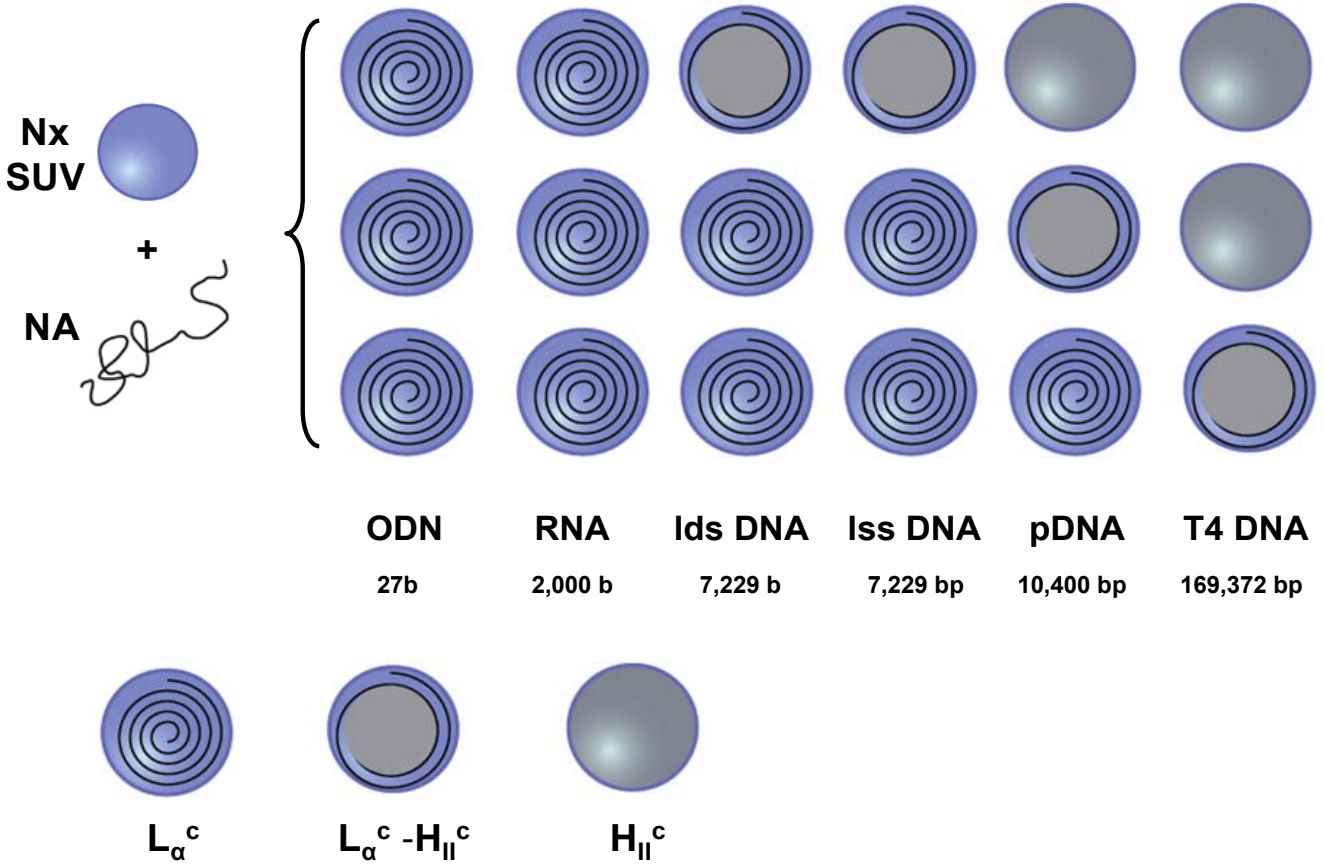
(Koltover et al, Biophys.J., 2000)

(Schmutz et al, PNAS, 1999)

II. Ulstrastructure of Lipoplex

Lipoplex formation: hypothesis



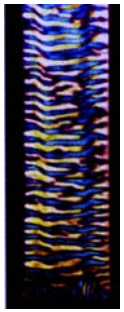


LIPOPLEX NANOSTRUCTURES REVEAL A GENERAL SELF-ORGANIZATION OF NUCLEIC ACIDS

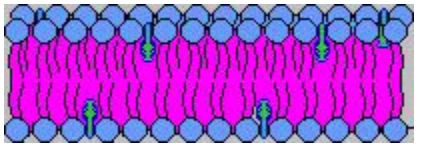
(Thierry A.R. et al, BBA, 2009)

I. Ulstrastructure of Lipoplex

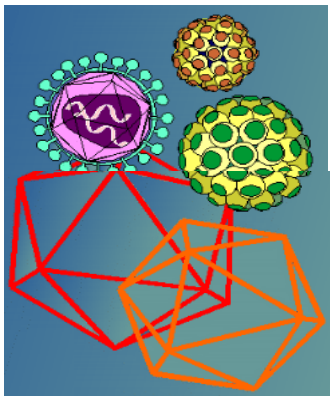
Lipoplex appears as a complex system



Lx is mainly based on molecular interactions

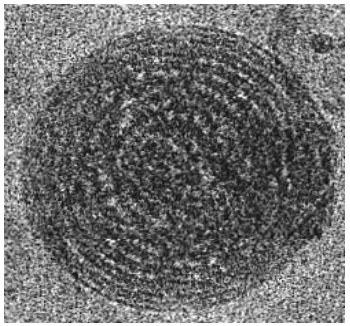


Self-organization in general, refers to the various mechanisms by which pattern, structure and order emerge spontaneously in complex systems.



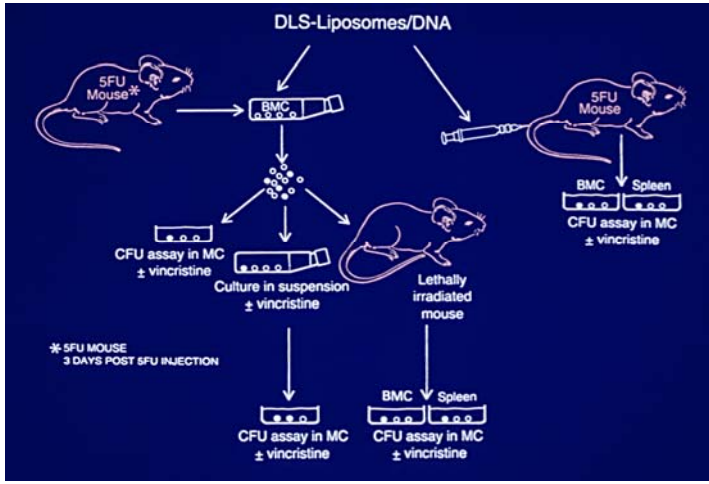
Self-organization appears to be an important mechanism useful for explaining pattern and structure in physical, chemical and biological systems.

1. Application to drug delivery nanotechnology
2. Artificial cell and prebiotic chemistry
3. Circulating DNA
4. Biosensor nanomachine



II. Application to experimental models for gene therapy

Lx as DNA delivery vector for gene therapy



Gene transfer:

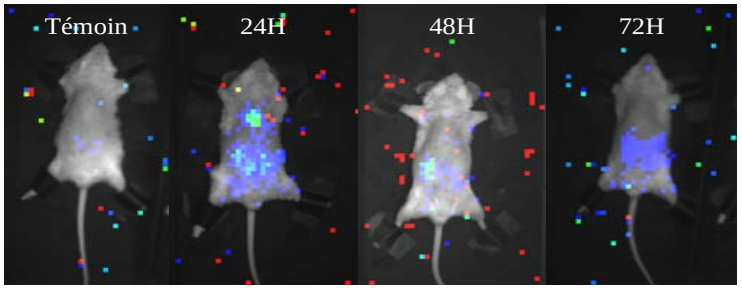
Characterization of liposome-mediated gene delivery : Expression, stability and pharmacokinetics of plasmid DNA
Gene Therapy 1997.

Systemic gene therapy : biodistribution and long-term expression of a transgene in mice.
Proc. Natl. Acad. Sci. USA., 1995.

In vitro and in vivo liposome-mediated gene transfer leads to human MDR1 expression in mouse bone marrow progenitor cells. Human Gene Ther. 1996.

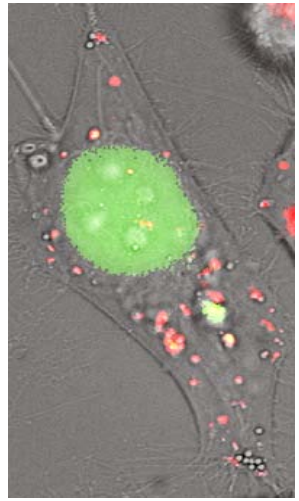
Expression of the Human Multidrug Resistance and Glucocerebrosidase cDNAS from Adeno-Associated Vectors : Efficient Promoter Activity of AAV Sequences and in vivo Delivery via liposomes. Human. Gene Ther. 1996.

Biodistribution de l'expression d'un transgène par détection en bioluminescence
Unpublished data, 2007



II. Application to experimental models for gene therapy

Lx as DNA delivery vector for oligonucleotides

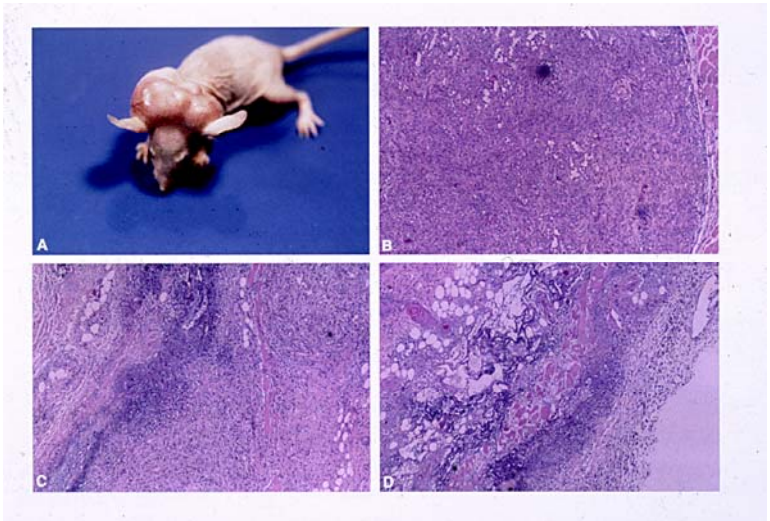


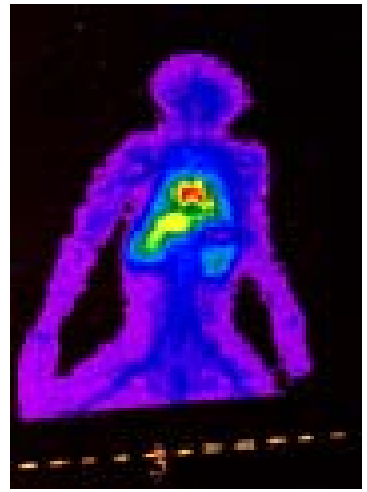
Transfert d'oligonucleotides:

Comparison of basic peptides- and lipid-based strategies for the delivery of splice correcting oligonucleotides. Biochim.Biophys.Acta, 2006

On the sequence specific activity of antisense oligonucleotides aimed at the inhibition of HIV-1 replication.
AAPS Pharm. Sci., 2002.

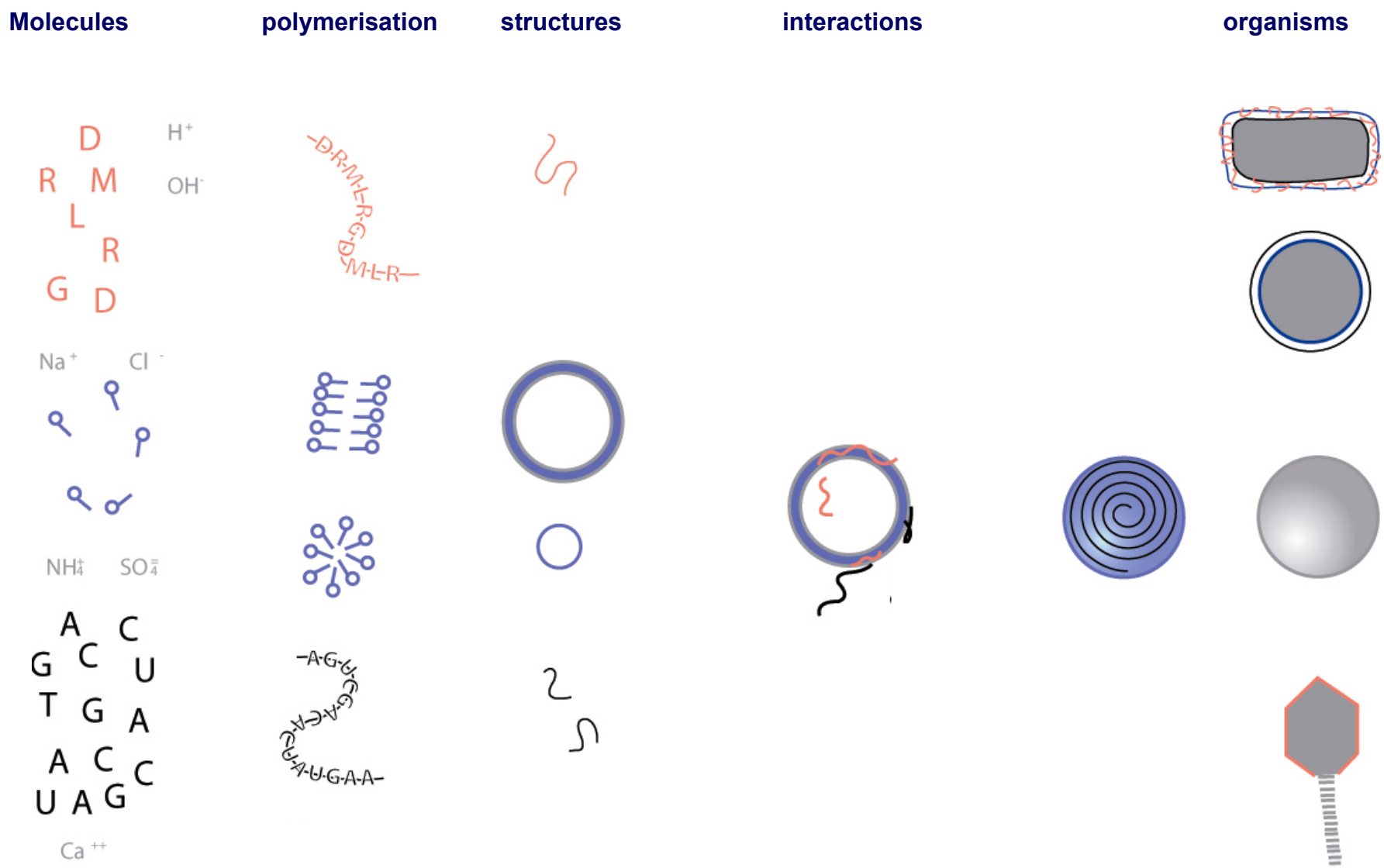
Cationic Liposomes/Lipids for Oligonucleotide Delivery: Application to the Inhibition of Tumorigenicity of Kaposi's Sarcoma by VEGF Antisense Oligodeoxynucleotides.
Method Enzymol. 2004





III. Research perspectives and implications

Lx as a prebiobiotic relevant model?



IV. Synthetic biology

Towards artificial cell

- How about self-organization in interaction such as in cell?
- Tensegrity and constraint
- Hardware of biochemistry: