# Beyond Nano-Sizing:
## Integrated Physico-Chemical Nano-Engines in Cosmeceuticals

Elishalom Yechiel, Ph.D.
President, Elsom Research Co., Inc.

**While nanotechnology is synonymized with particle downsizing, such a view is simplistic. New challenges in nanotechnology require the development of nano-tools and integrated and synchronized nano-array molecular arrangements. Such structures may perform as physico-chemical nano-engines in skincare products, by sequentially mobilizing, translocating, and targeting actives to multiple locations.**

# Key Concepts:
## "Nano-" Has Become Hype

The current shining halo of everything related to nanotechnology, and the successful marketing edge of companies with nanotechnology capabilities is creating a "nanotechnology rush", where many companies are seeking to use the term "nanotechnology" in describing their products. Consequently, the term has been popularized to some degree and is broadly and inappropriately used as a synonym of downsizing.

# Key Concepts:
## Size is Not the Whole Story

While downsizing can legitimately be an aspect of nanotechnology, there is more to it than the downsizing issue. “Nano-” describes a specific, small size, of less than a micron; “-technology” refers to human inventiveness.

Example: mixing sugar crystals in water breaks down the crystals into individual molecules which approach the sub-nanometer size. **Is mixing sugar in water “nanotechnology”?** The answer is obvious: nanotechnology is not just small size, but also requires a technological solution to a problem. Since mixing sugar in water does not have a technological component, the nano-sizing of sugar crystals is not nanotechnology.

# Key Concepts:
## New Tools are a Big Part of the Story

Another example is downsizing silica crystals. Since silica crystals can be downsized to as low as 50 nanometers by mill grinding, downsizing silica crystals to 50-nanometer size cannot be called “nanotechnology”. However, in creating silica of 10-20 nanometer size, different and complex technologies had to be developed to replace mill grinding. Since these technologies are not obvious, it is possible to describe the 10-nanometer silica crystal development as nanotechnology.

# Key Concepts:
## Special Tools Required For Specific Applications

Another aspect of nanotechnology is that tools have to be created simultaneously with their application. Example: to insert a nail in wood, one can use an hammer. If the nail is several molecules in size, a special hammer must be developed at the same time that such a small nail is developed. In addition, positioning tools for the nano-nail must also be created so that it can be directed to its target in the proper orientation. A variety of similar challenges are created by the need for nano-manipulation.

# Beyond Nano-Sizing:
## Key Concepts

Among the nanotechnology-related principles and applications which will be discussed in this presentation are:

- **Downsizing Beyond Current Limits and Technologies**
- **Symmetric and Asymmetric Molecular Nano-Array Structuring**
- **Molecular Array Shape Shifting**
- **Multiple Target Identification**
- **Multiple Barrier Crossing**
- **Selective Dispensing of Actives at Multiple Targets**
- **Nano-Tool Creation**

The above challenges in nanotechnology-enhanced topicals could revolutionize the current view of topicals by introducing new possibilities such as multi-step, highly flexible, and interactive delivery systems that can sense and negotiate problems.

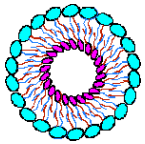
# Nanotechnology is Not New
## Except For The Name

## Nanotechnology in Ancient History

# Nanotechnology is Not New
## Except For The Name

## Nanotechnology in Modern Science

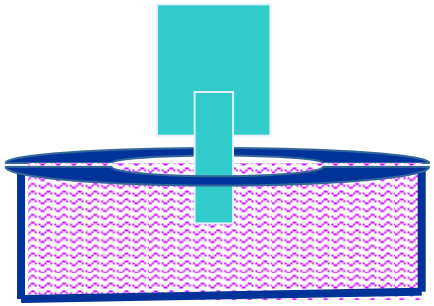
**Small Liposomes**



**Solid-Phase Synthesis**

Cyclic and Branched Polymers
Racemization Control
Solubility Restrictions

**Ultrasonically Enhanced Chemical Synthesis**



# Nanotechnology in Downsizing
## When Downsizing Requires New Technologies

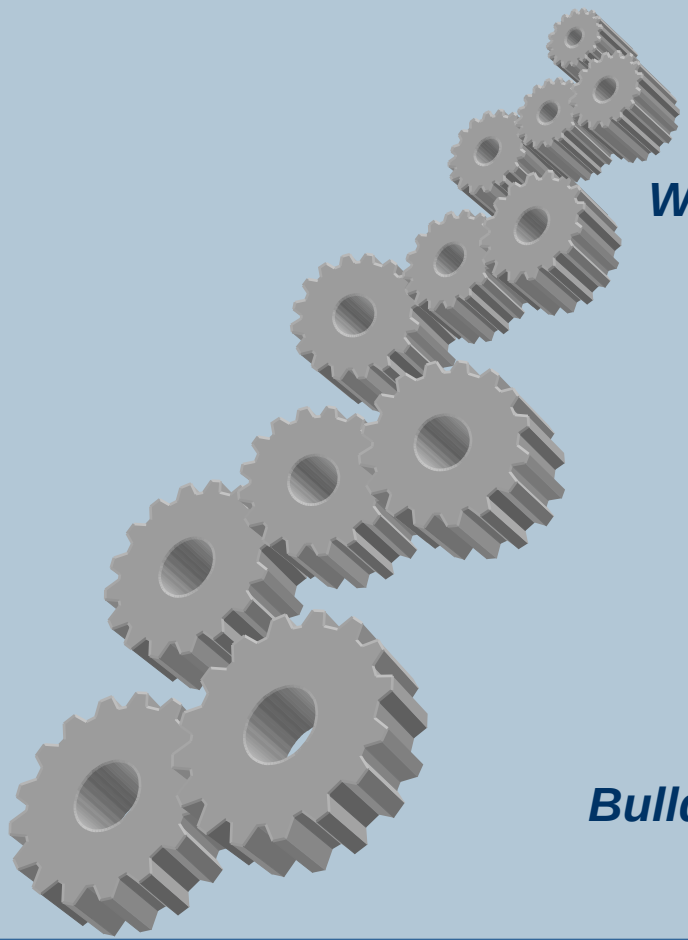
Visible-Range Technology

Micrometer-Range Technology

**The Technology Barrier**

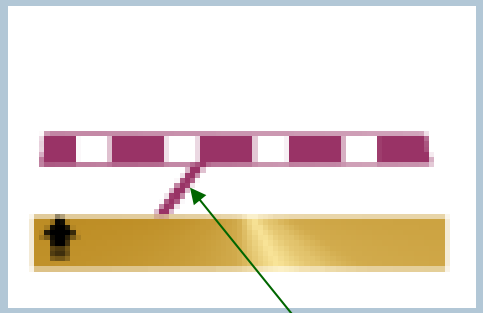
Multiple Parts

Few Parts



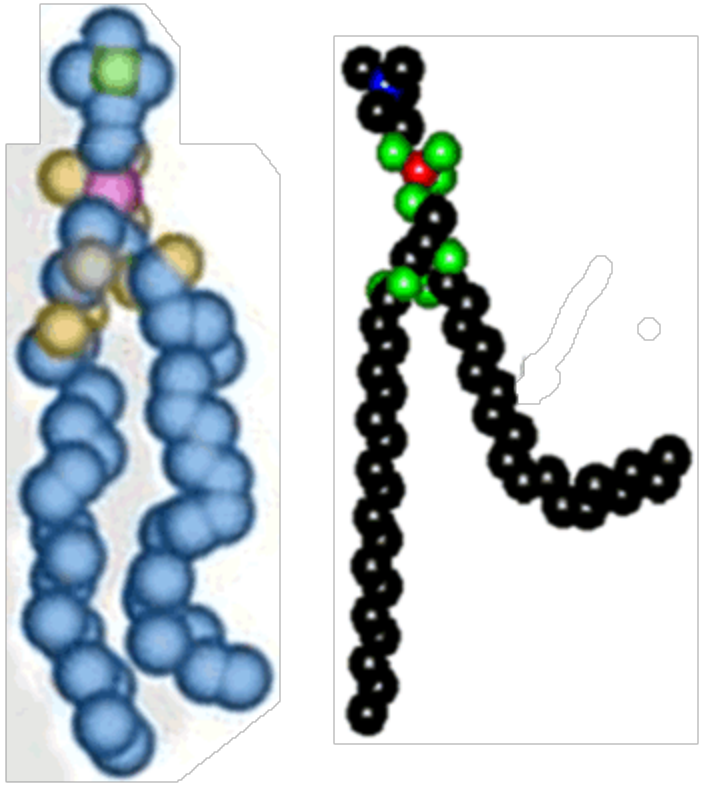
***Watch*** Gears

***Bulldozer*** Gears



Micrometer-Range Size

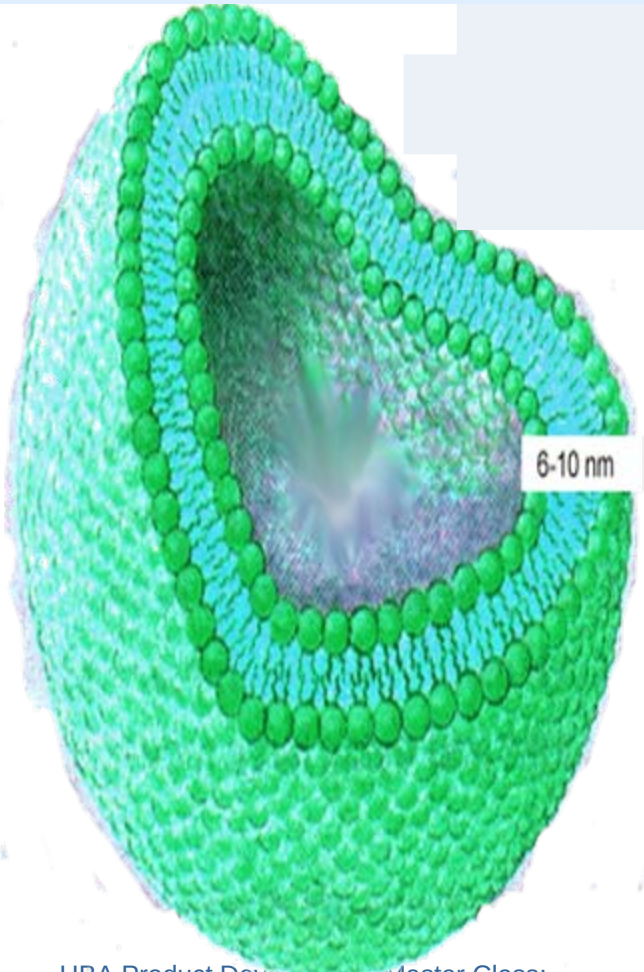
# Nanometer-Range Technology



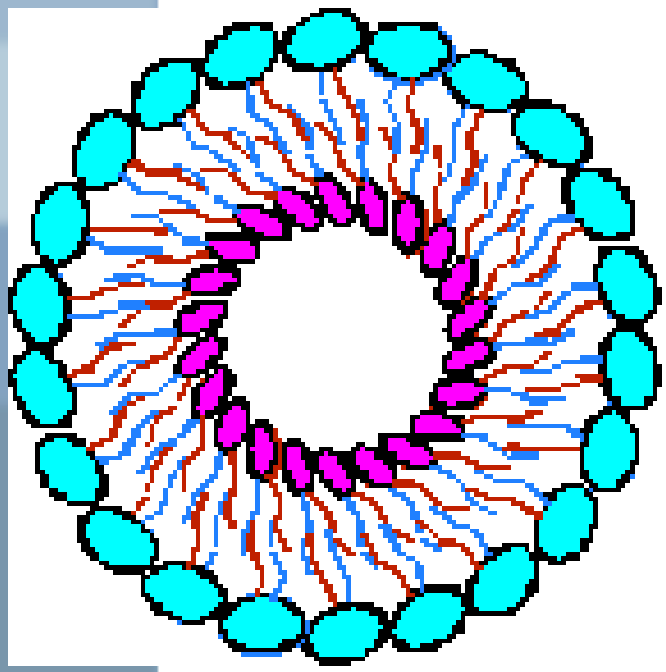
# Size is Part of The Story

- **The plasma membrane is only about 2.25% of the total membrane surface in the cell.**
- **The endoplasmic reticulum membrane surface is 45 times larger than the plasma membrane surface area in a human cell.**
- **Lipid bilayer plasma membranes are 6-10 nm thick.**
- **The major membrane lipids are phospholipids.**
- **Fatty acid chains are in the range of 16-18 carbons long.**
- **Chains with fewer than 12 carbons cannot form a stable bilayer.**
- **The phospholipids in cell membranes self-organize in water into a bilayer formation.**
- **One square nanometer will only contain about one phospholipid molecule.**
- **A cell membrane may contain approximately 10 billion lipid molecules.**

# Medium-Sized Unilamellar Liposome



# Nanosome™
# Very Small Liposome

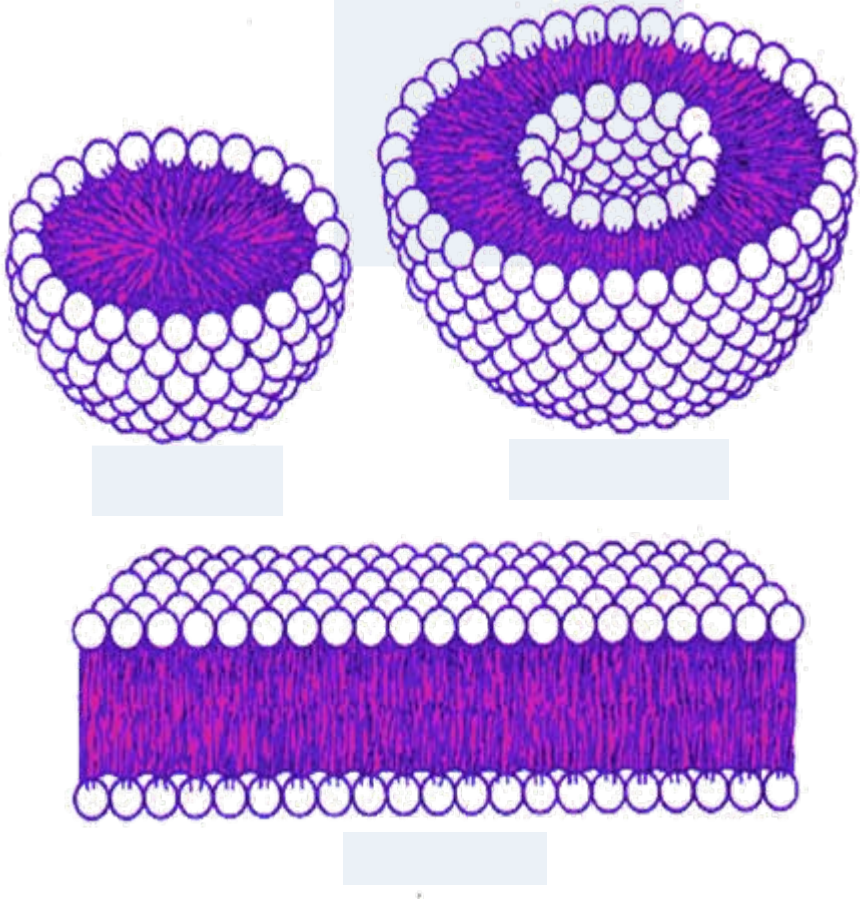


**The smallest liposome is estimated to be 20 nm.**

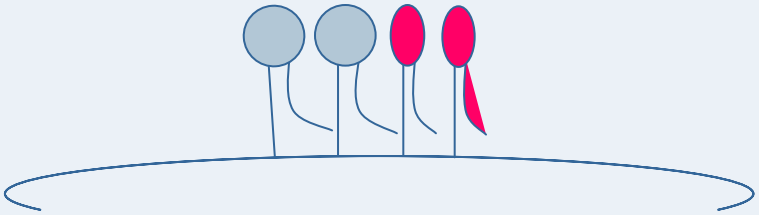
**Size is limited by physical constraints of angular lipid positioning.**

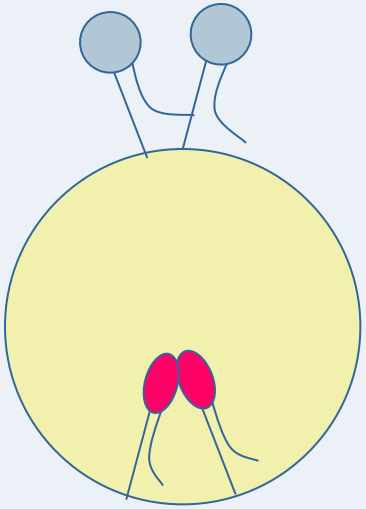
**Phospholipids with small head-groups will prefer the inner leaflet**

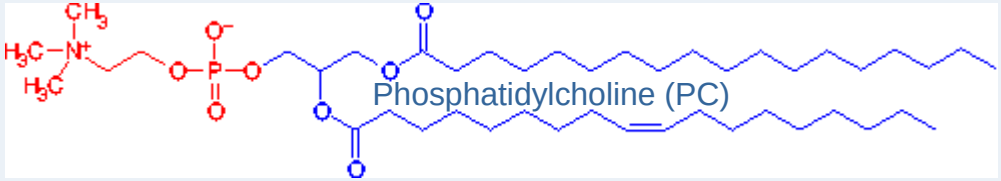
# Liposomes, Micelles, and Bilayers

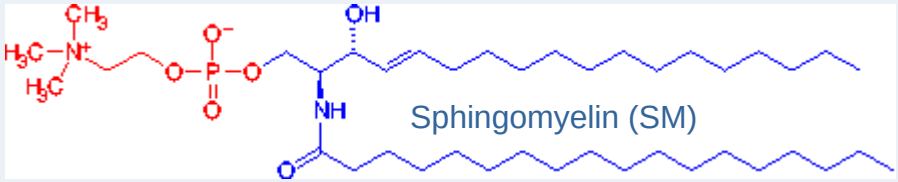


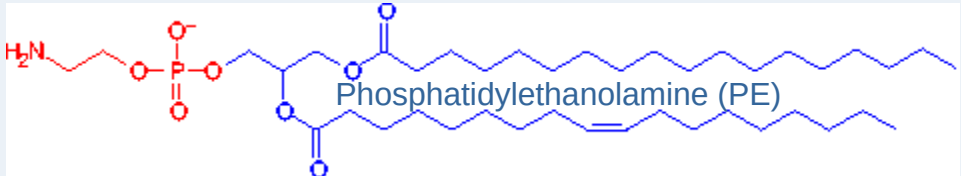
# Angular Packing and Liposome Stability

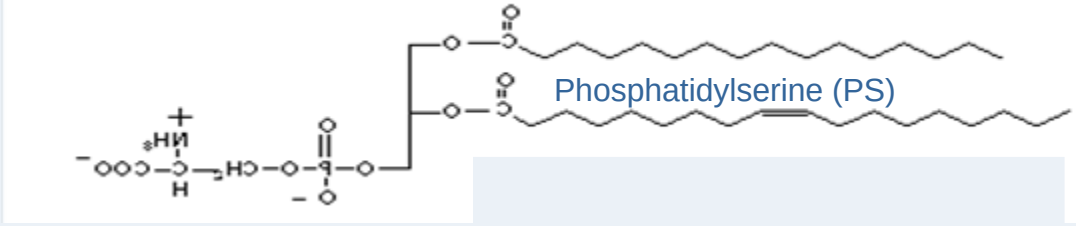






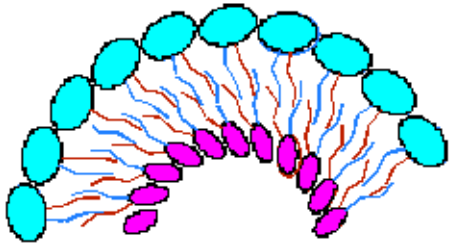



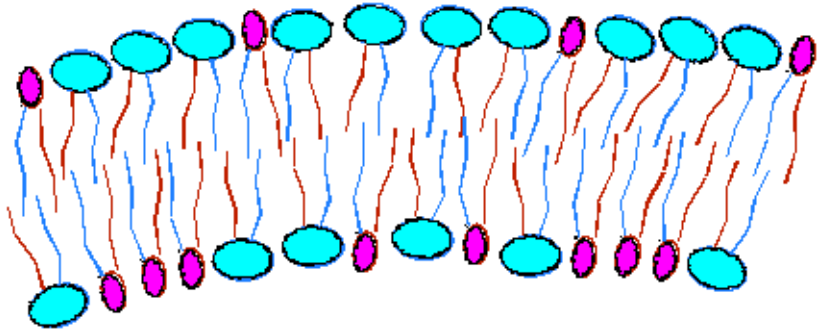

PC, SM

PE, PS

# Lipid Asymmetry



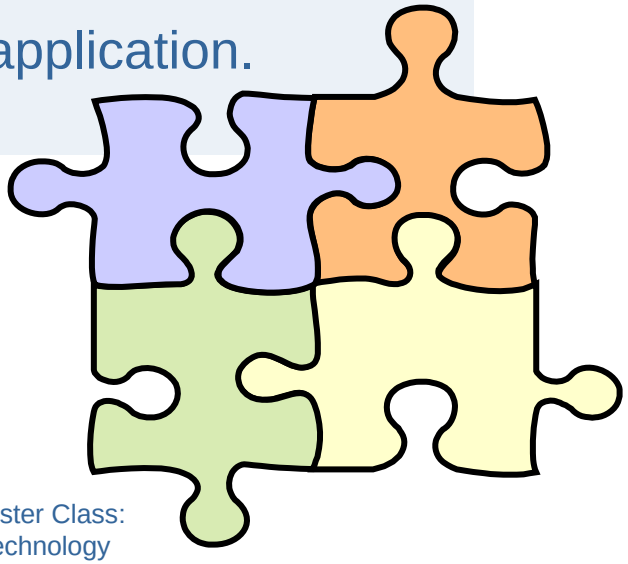
Very Small Liposome
(Nanosome) Formation



Cell Membrane Formation

# Nanotechnology Beyond Downsizing

- The critical size limit which defines nanotechnology is different for each application.
- No general tools available.
- Specific tooling design per specific application.
- The technology component is critical to the application.



# FOR MORE INFORMATION

- Physico-chemical nano-engines will be discussed in detail in the online *Journal of Topical Formulations* October 2006

- Contact me
  - innovation@elsomresearch.com
  - 210.493.5225