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Yeast Cell Walls as an Encapsulation platform for Biopesticides

Clive Newitt - CEO

Eden Research plc

THE COMPANY AND ITS TECHNOLOGIES

- **Eden Research is an intellectual property company with two patented encapsulation delivery systems as its core technologies**
- **Our products, based upon terpenes, part of the natural defence mechanisms of plants, are joined with the encapsulation system enabling these active substances to be delivered in a controlled manner, over a period of time**
- **The applications for these technologies include:**
  - **Crop Protection** – *wine, fruit, flower and vegetable industries*
  - **Animal health** – *flea and tick treatments, animal shampoos*
  - **Biocides** – *ant and cockroach killers, mosquito control*
  - **Cosmetics** – *perfumes, skin and hair products*
  - **Human health** – *head-lice*
  - **Food** – *food flavourings and preservatives*
- **Applications are developed through innovative research and commercial production, marketing and distribution partnerships**

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THE CHALLENGES AND A SOLUTION

THE CHALLENGE FOR BIOPESTICIDES

- **Harnessing naturally active substances and organisms that may be fragile, or UV unstable in a user friendly formulation**
- **Plant extracts can be too volatile, short-lived, in-soluble and potentially phytotoxic in high doses**

THE SOLUTION

- ***We have a solution for hydrophobic molecules allowing them to be commercially usable and viable with our patented encapsulation delivery system!***

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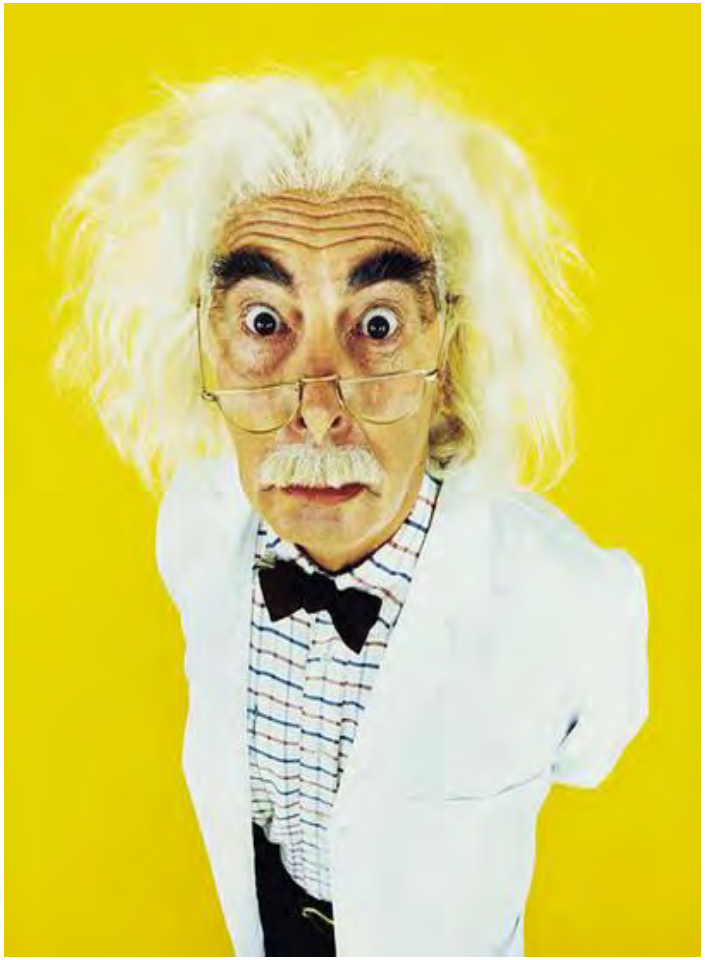
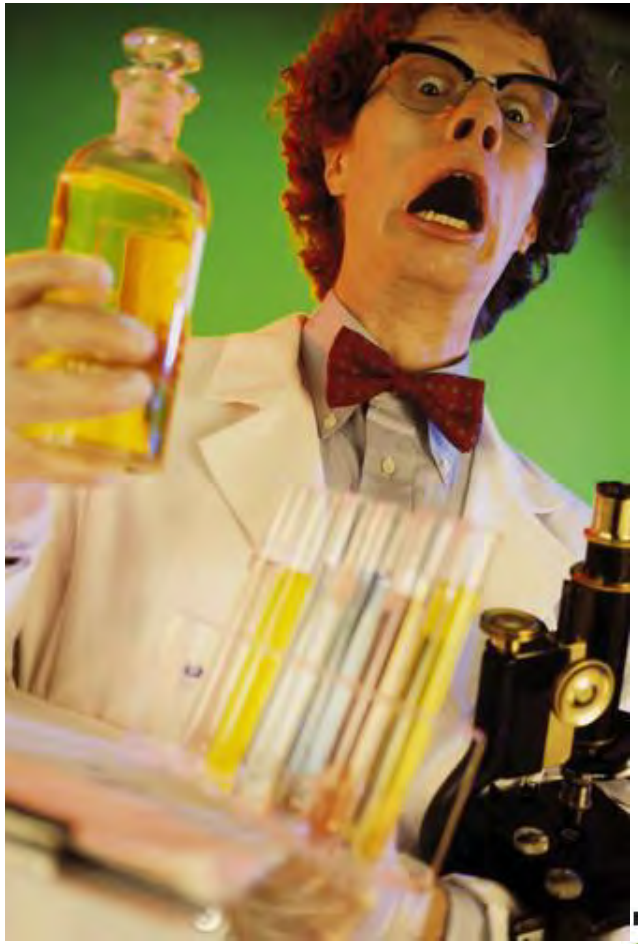
Formulation – Science or Dark Art?





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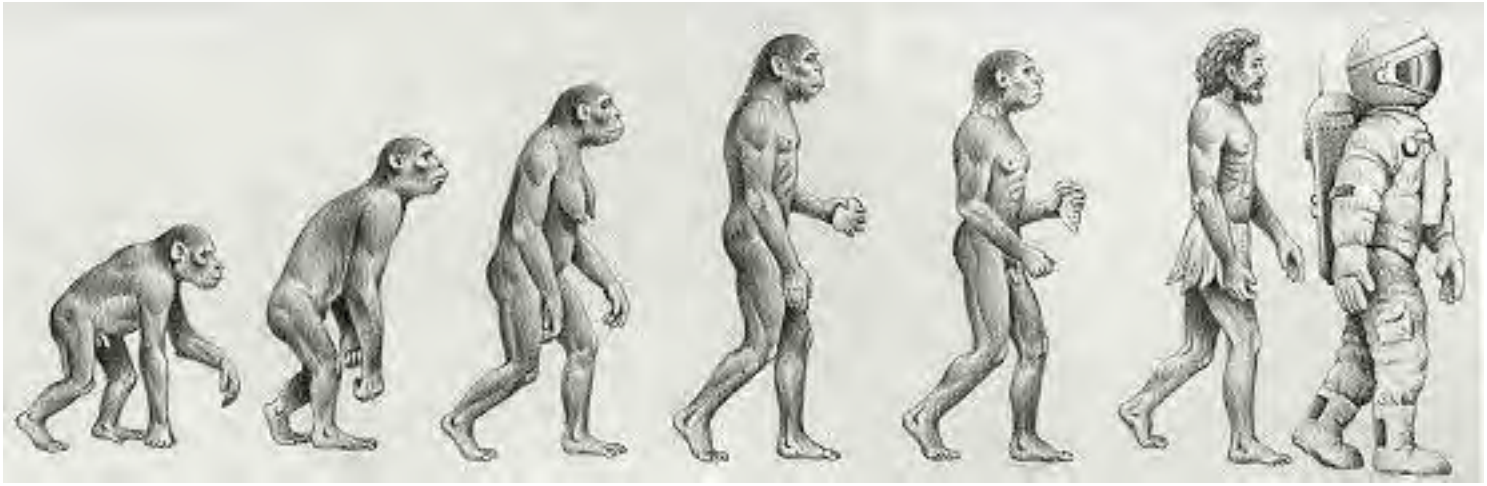
Formulation Development



From WP's to SC/EC to SE/EW to WDG's & ME's

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TERPENES

- Terpenes - naturally occurring plant defence chemicals found in plant essential oils
- Terpenes are derived biosynthetically from units of isoprene, which has the molecular formula C_5H_8. The basic molecular formulae of terpenes are multiples of that, $(C_5H_8)_n$. Monoterpene structure is $(C_5H_8)_2$
- Broad antimicrobial, antifungal anti-nematicidal and insecticidal activities
- Historically, commercial use limited due to:
  - poor water solubility
  - volatility
  - phytotoxicity

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TERPENE TECHNOLOGY

- From early research, multiple product possibilities through different combinations of two or more terpenes have been identified
- Thymol (thyme oil) *
- Eugenol (clove oil) *
- Geraniol (rose oil) *
- Citral (lemongrass oil)
- Carvone (mint oil)
- But needed to find delivery platform!

* Eden EU dossier for active substance

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ENCAPSULATION TECHNOLOGY

- Searched via Technology “Scout” for natural system
- Yeast Cell Technology existed (MICAP plc) but load capacity very limited and release required destruction of cell
- Partial Yeast Cell Technology developed in Pharma area by Professor Gary Ostroff*
- Process validation project commenced in 2004
- Patent rights acquired for all applications ***except*** Pharma by Eden Research

** Now Research Professor at UMMS, Worcester, USA*

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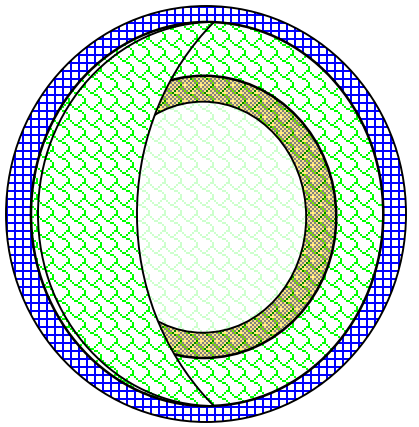
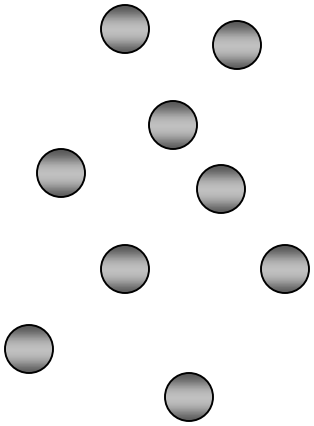
Terpene Loading into YPs

Yeast Particle

(YP)





Terpene Payload

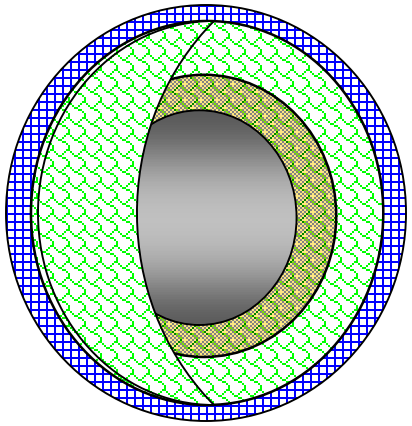
Aqueous emulsion

Microemulsion

Formulation

Passive diffusion

YP Encapsulated Terpene



Terpene payload encapsulated into hollow sphere (>95%)

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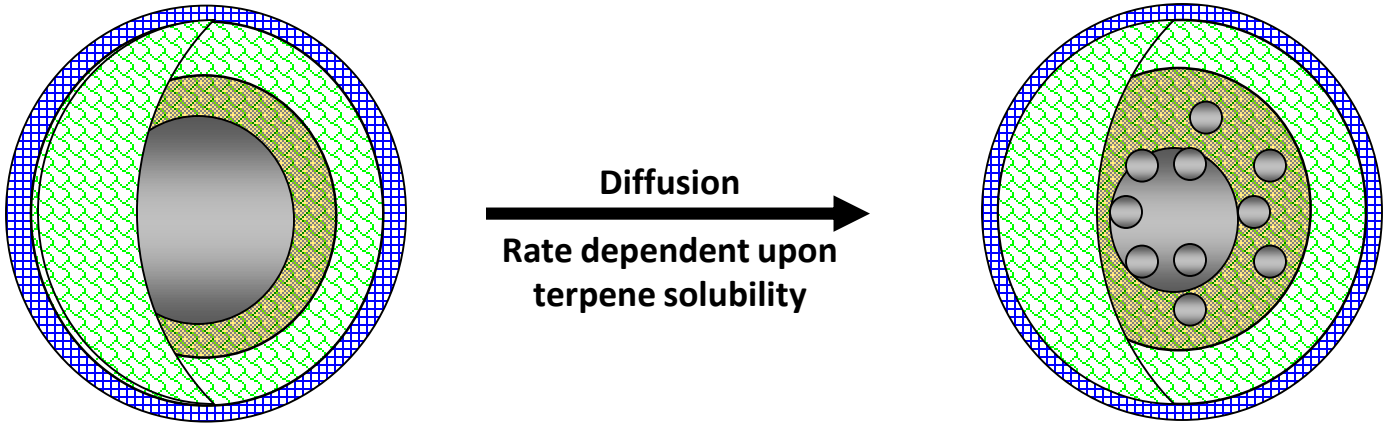
Terpene Release from YPs

YP Encapsulated Terpene



Encapsulated terpene payload diffuses from internal YP cavity to aqueous phase outside sphere

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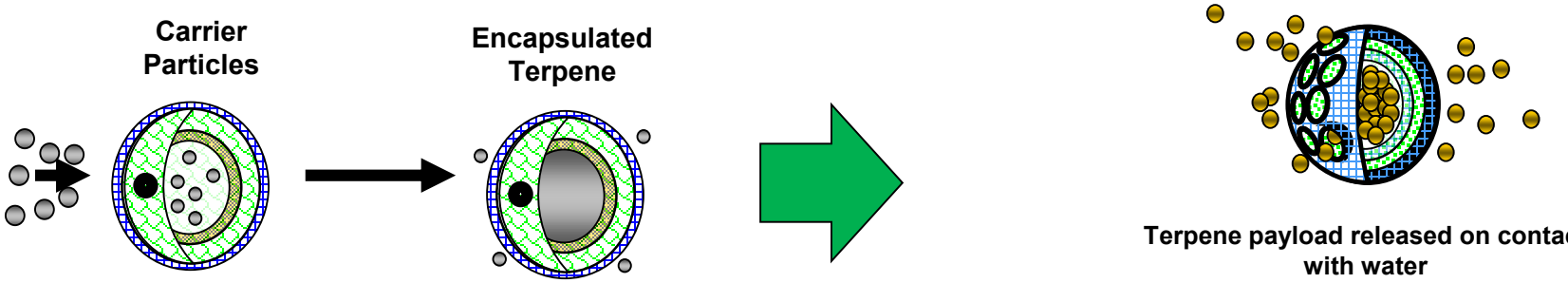
EDEN'S PATENTED ENCAPSULATION SYSTEM – "TECHNOLOGY ONE"



- Encapsulation enables slowed release – determined by water solubility(upto 14 days)
- Formulation enhances efficacy up to 4 fold compared to unencapsulated!
- Loading efficiency >95%, minimal capital investment required!
- Encapsulation Patent granted in New Zealand, Australia, China, Mexico, Singapore, South Africa and EU, with other claims in process
- Formulation patents in various stages of approval (Fungicidal, insecticidal and nematicidal compositions)

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ENCAPSULATION TECHNOLOGY

Yeast Cells

- Waste food grade material sourced from Baking, Brewing and/or Bioethanol industries
- Specification is the key – residual lipid membrane
- Can load upto 2g per gram of cells
- Passive encapsulation system for hydrophobic molecules
- Stable over wide pH range (2-11)
- Temperature stable upto 200°C, 5000psi and Sonicator stable
- Development products are 16.5% ai content (can increase to 30%)

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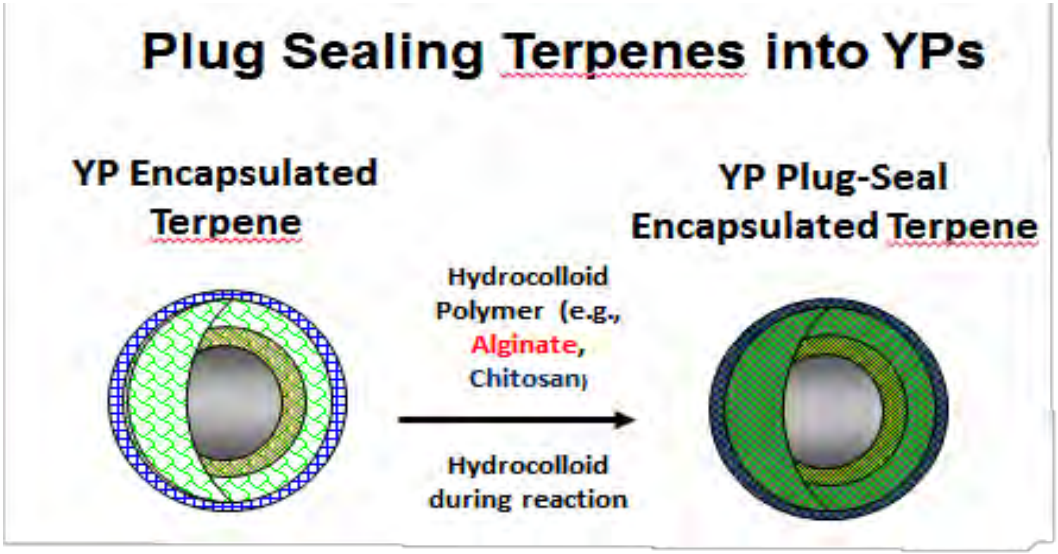
EDEN'S SECOND GENERATION ENCAPSULATION SYSTEM "TECHNOLOGY TWO"



- "Technology Two" provides greater control and increased delay over the release of active substances by using bio-polymers
- The patent behind the licence has been granted in 8 countries including USA, Italy, France and Spain with applications progressing in further territories

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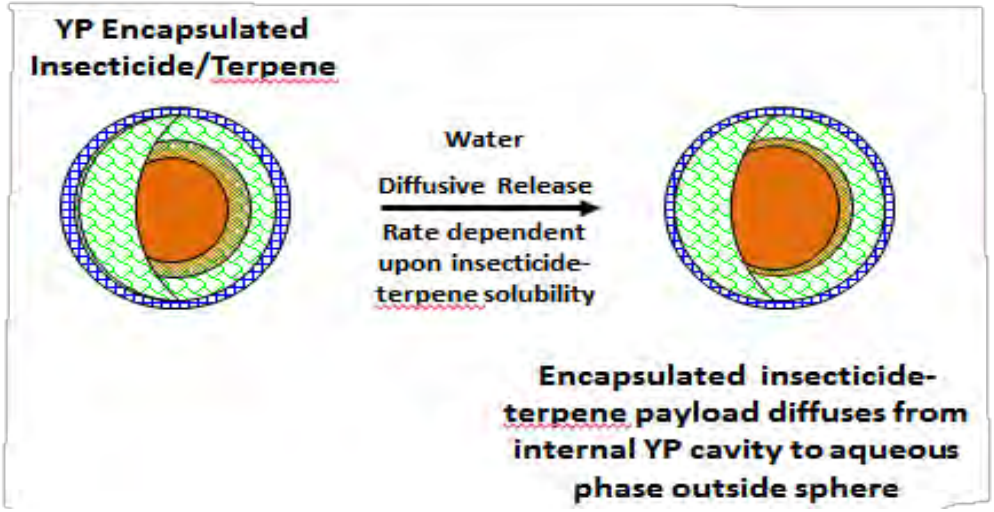
CROP PROTECTION OPPORTUNITIES

CO-ENCAPSULATION



- It is also possible to co-encapsulate other actives (non-terpenes), with the terpene component acting either as a co-active or carrier
- This allows Eden to use its encapsulation technologies as a platform to give valuable advantages to existing products:
  - Providing residual effect/Improved handling characteristics
  - Tackling resistance build-up experienced by older molecules
  - Providing further possible IP protection

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So Simple?

- **Need to understand solubility co-efficients of materials**

- **Need to know MIC levels required for target**

- **Need to balance free vs encapsulated payload**

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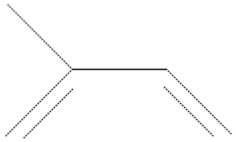
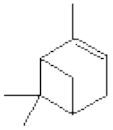
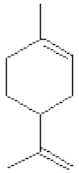
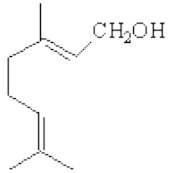
Eden's Dilemma……Exploitation?

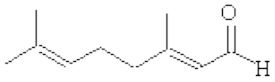


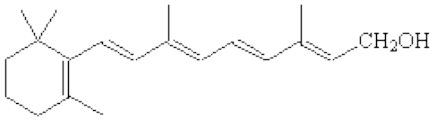
isoprene

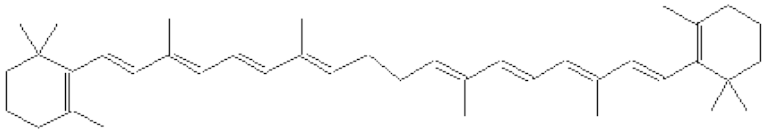
α-pinene 

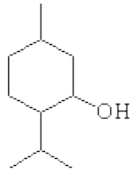
Limonene 

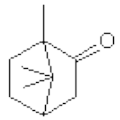
Geraniol 

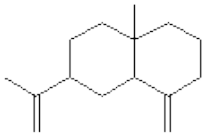
Citral 

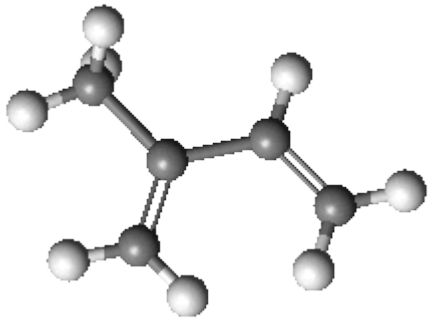
Vitamin A (Retinol) 

β-carotene 

Menthol 

Camphor 

β-selinene 



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EDEN'S FOCUS

- **Multiple product possibilities through different combinations of two or more Class 25b terpenes**
  - **Thymol (thyme oil)**
  - **Eugenol (clove oil)**
  - **Citral (lemongrass oil)**
  - **Geraniol (rose oil)**
  - **Carvone (mint oil)**
  - **Carvacrol (oregano oil)**

*** Experience with linalool, limonene, tea tree oil, lavandin, borneol…..**

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CURRENT EDEN DEVELOPMENTS

- 3 Active substance dossiers submitted via CRD plus Reference formulation dossier (3AEY) in 2008!
- EFSA review concluded 12th October 2012 with positive Commission vote on May 16/17 2013
- First global registration expected in Kenya 2013
- Zonal submission made September 2013 for 3AEY, Biological dossier for nematicide 70% complete (GT)
- Product Technology out-licensed in Animal Health, Human Health
- Platform Technology projects with 3rd party actives
- Access agreements to EU dossiers

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High Yeast Particle Loading Capacity

- **>10^6 plasmid molecules** (**Soto and Ostroff,** Bioconj Chem (2008), 19(4), 840-848)
- **>10^8 siRNA/oligonucleotides** (**Aouadi et al., Nature 458(7242), 1180-1184**)
- **>10^7 protein molecules** (**Huang et al, 2010. mBio.00164-10**)
- **Up to 200% w/w small molecules, oils**
- **>10^5 nanoparticles** (**Soto et al,** Journal of Drug Delivery (2012) doi:10.1155/2012/143524)

YPs are a versatile, natural, high capacity, cost-effective delivery system.

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