What is Happening to Nanotechnology in Agrochemical Formulation?

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What is Happening to Nanotechnology in Agrochemical Formulation?

- Nanomaterials: Definition
- Nanoparticles
  - Properties
  - Applications
  - Challenges: Stability and Safety
- Other Nanomaterials
- Nanotechnology in Agrochemicals
  - Review of some examples
  - Patents and publications
- Conclusions and Discussion Points

Nanomaterials - Definitions

"Nanomaterials are chemical substances or materials that are manufactured and used on a very small scale. Their structures range from approximately ***1 to 100 nm in at least one dimension****"* (ECHA)

"A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for ***50 % or more of the particles*** *in the number size distribution,* ***one or more external dimensions is in the size range 1 nm - 100 nm.***

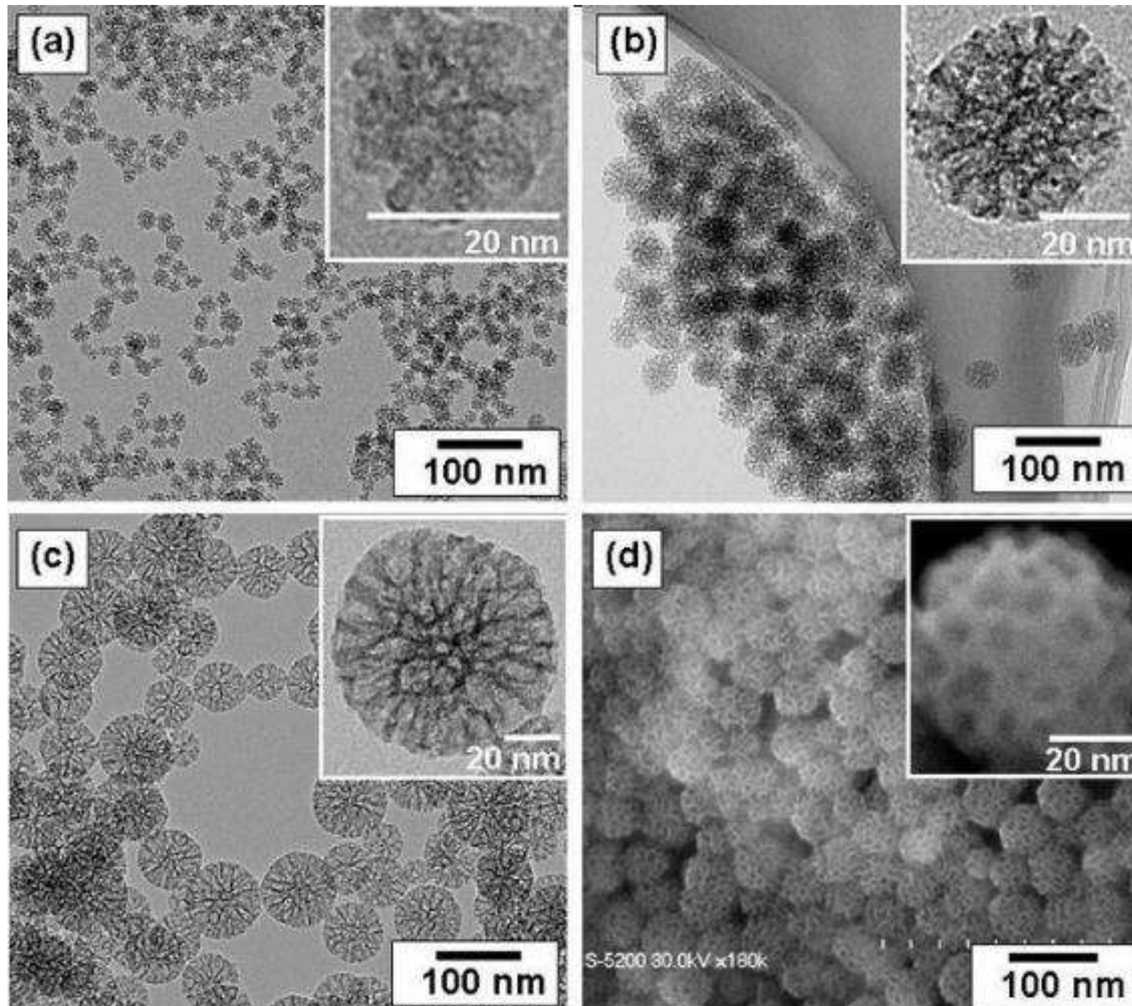
In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution ***threshold of 50 % may be replaced by a threshold between 1 and 50 %.***

*…**fullerenes, graphene flakes and single wall carbon nanotubes** with one or more external dimensions **below 1 nm** should be considered as nanomaterials."*

(EU 2011)

Nanoparticles

- All three dimensions are nanoscale
- Often made via "bottom-up" synthesis, e.g. via a precipitation reaction
- Sometimes "top-down" manufacture, e.g. wet milling



Some Other Nanomaterials

- **Nanosurfaces**
  - Surface modification with nanoscale roughness
  - E.g. preventing adhesion of dirt, microorganisms
- **Nanotubes**
  - E.g. carbon nanotubes
- **Low dimensional solids**
  - Only one dimension is nanosize
  - Platelet structures, e.g. graphene, nanoclays

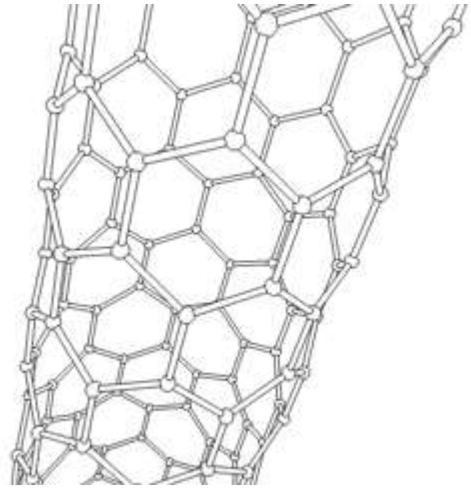


Image: Schwarzm - licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license https://en.wikipedia.org/wiki/File:Kohlenstoffnanoroehre_Animation.gif

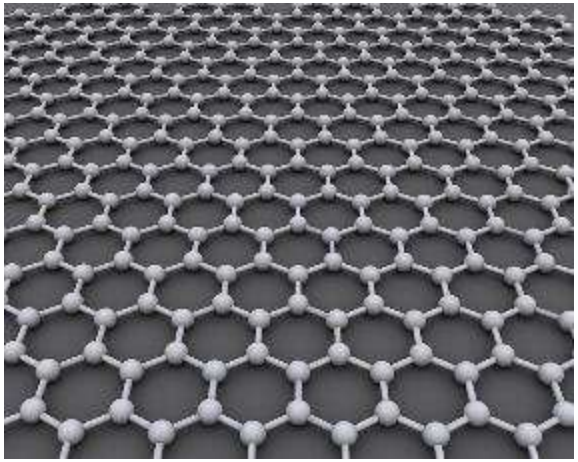
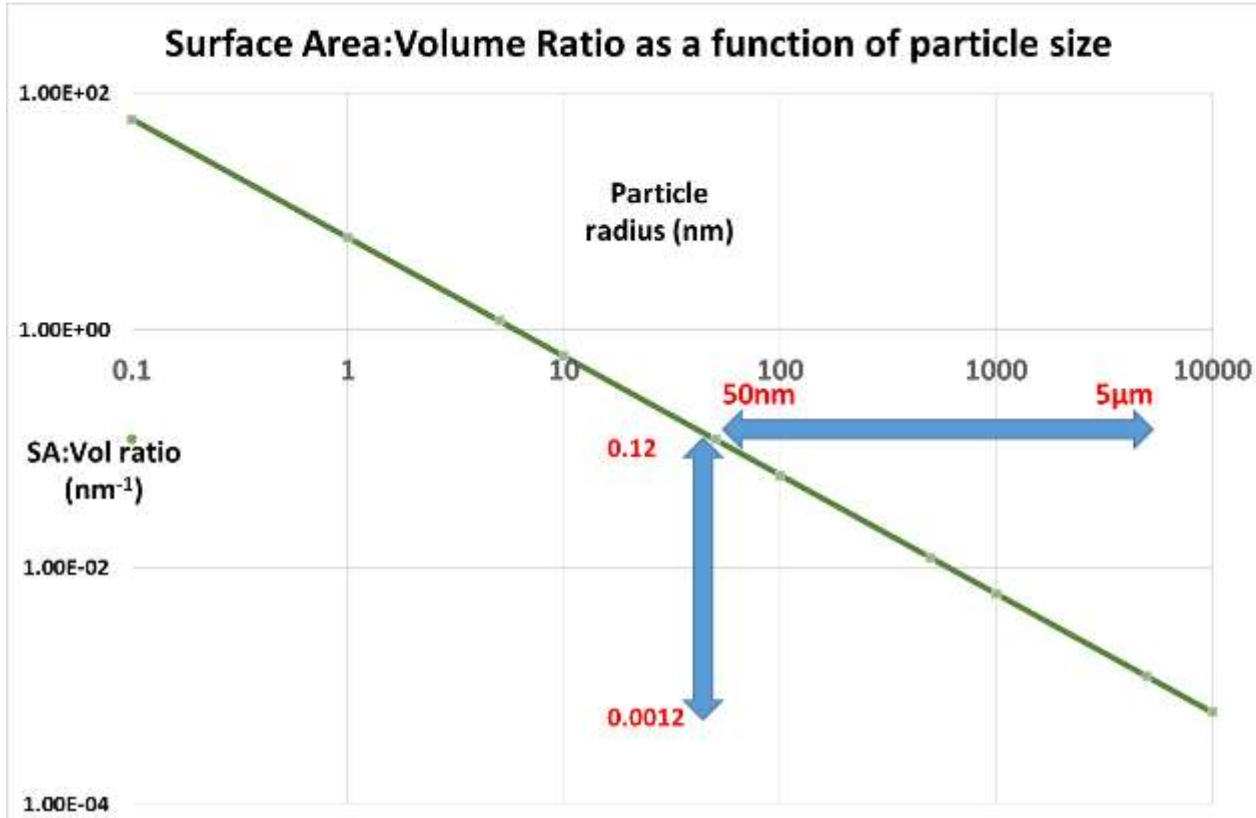


Image: AlexanderAlUS - licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license https://en.wikipedia.org/wiki/File:Graphen.jpg

Nanoparticles: Some Properties

Very high surface area:volume ratio

- 50nm particle contains approx. 200,000 molecules
- 5µm particle contains approx. 200,000,000,000 molecules



Higher solubility and rate of dissolution

$$\ln\left(\frac{S_r}{S_\infty}\right) \propto 1/r$$

S = solubility, r = particle radius

$$\frac{dC}{dt} \propto A\ (S\text{-}C)$$

C = concentration, A =surface area

Applications – General

- Nanoparticles are not new.
  - Many conventional organic and inorganic pigments are in the nano size range, and always have been
  - Naturally occurring materials can consist of particles or droplets in the nano size range – e.g. milk
- Medicines – Targeted delivery and release
- Printed electronics
- Displays – quantum dots
- Sunscreens
- Ink jet printing
- Agrochemicals

Nanoparticle Challenges – Stability

- Finer particle-sized dispersions have a lower tendency to settle (Stokes' Law), but…
- As with all particle dispersions, nanodispersions will tend to flocculate and aggregate
- Thermodynamics: Particulate systems tend to move towards state of lower free energy

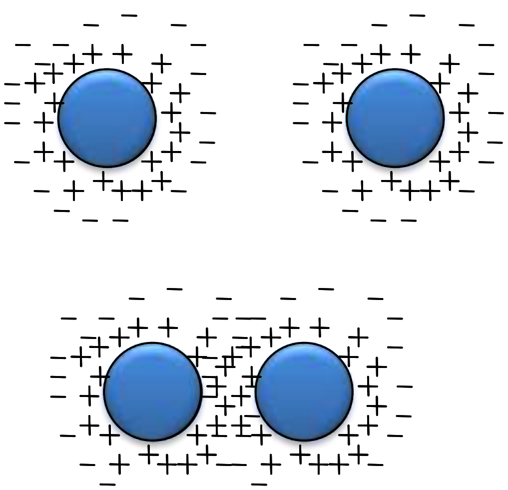
  → **Acts to reduce surface area, i.e. form larger (aggregated) particles**
- The higher the (specific) surface area of the particles, the higher the driving force for aggregation

  → **Nanoparticles are more challenging to disperse, and to keep dispersed, than microparticles.**

Electrostatic/Steric Stabilisation

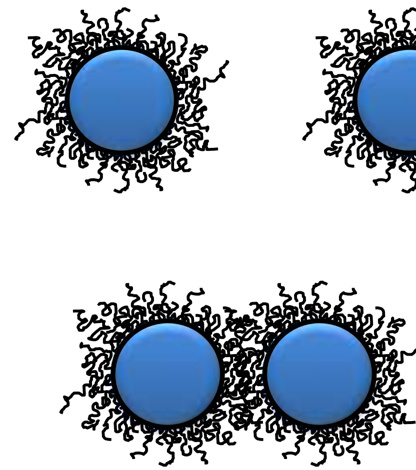
Two main ways of keeping particles apart

Electrostatic potential



Coulombic repulsion → electrostatic stabilisation

Steric potential

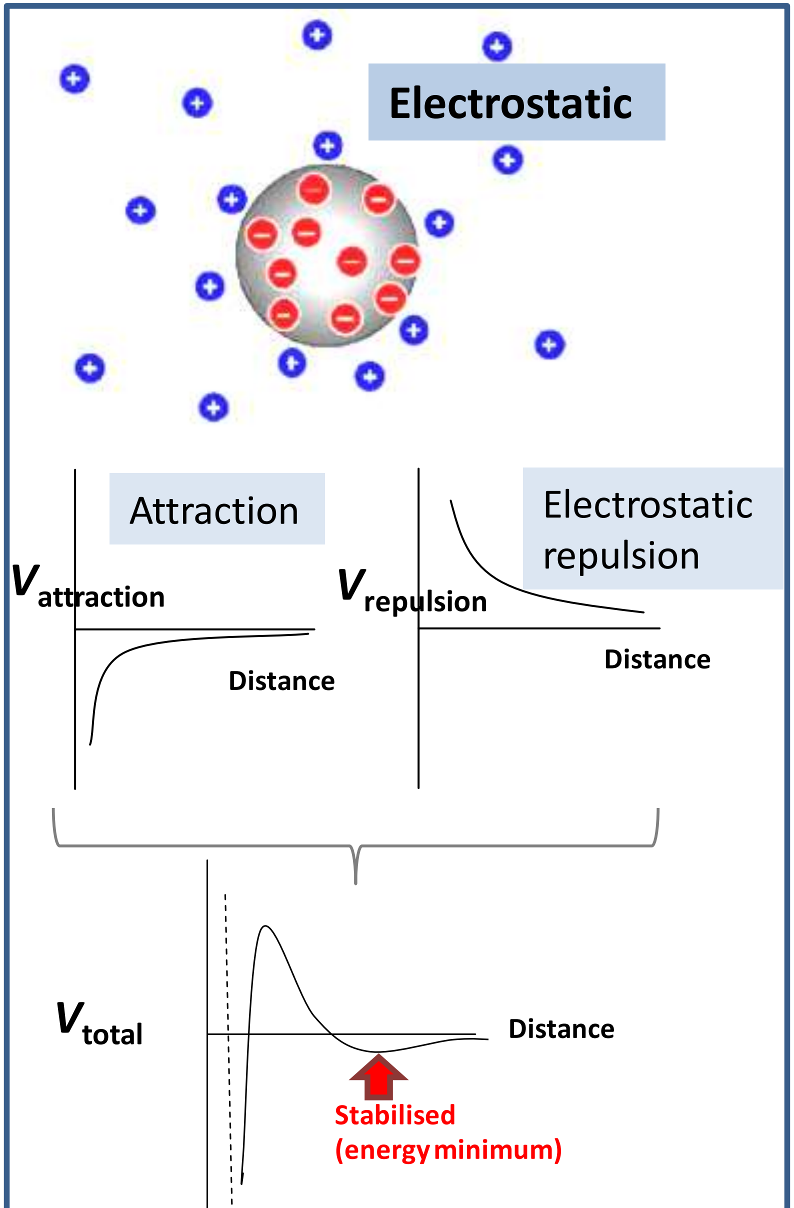


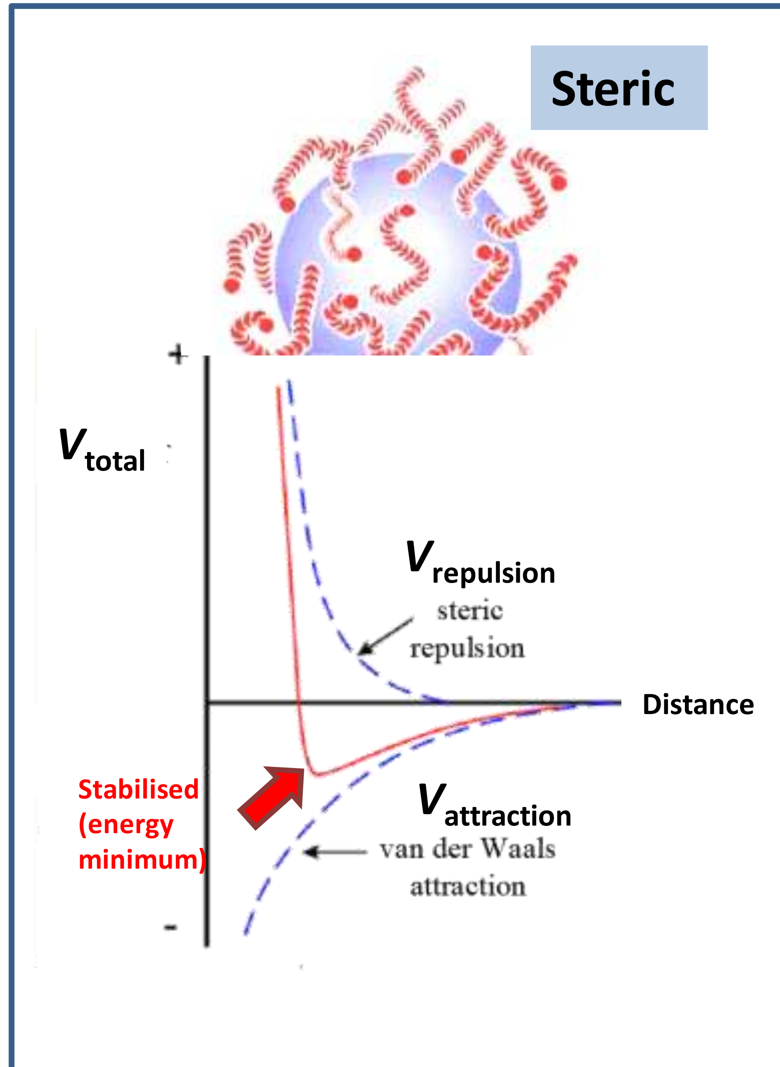
Entropic hindrance → steric stabilization

Thermodynamics: Entropy favours the less ordered state, i.e**. polymer chains not mingling**

Nanoparticles: High surface area causes a high van der Waals attraction

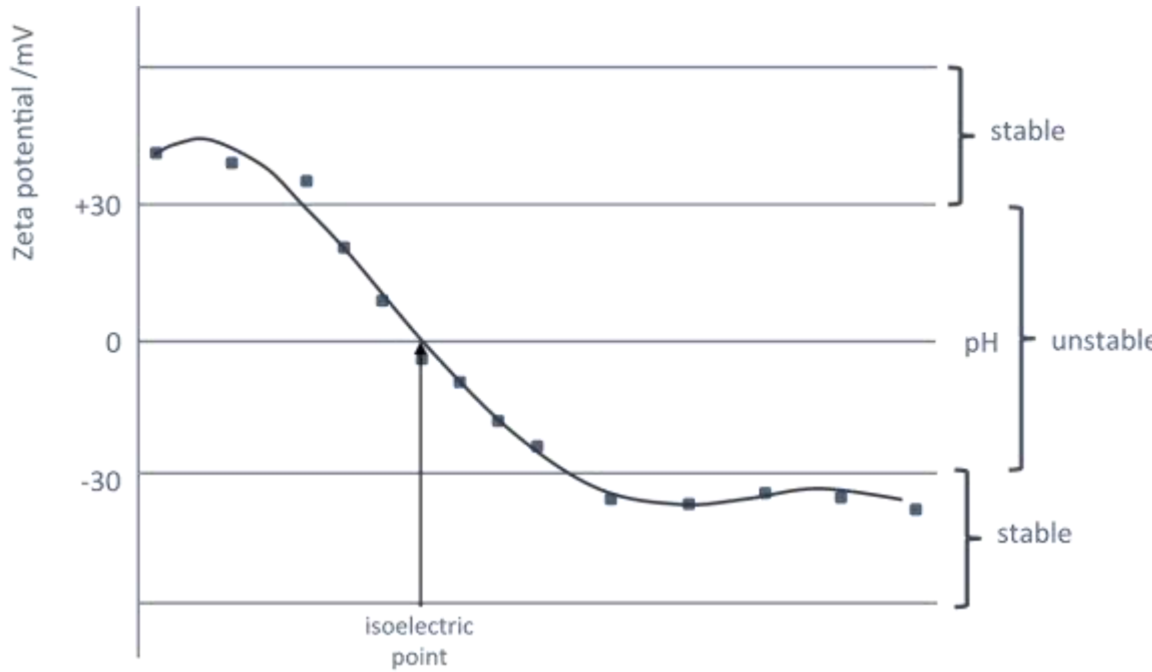
$$V_{total} = V_{attraction} + V_{repulsion}$$





Application of Zeta Potential (ζ)

- Large negative (-30mV) *or* positive (+30mV) ζ means dominant electrostatic repulsion
- Small ζ ⇒ means dominant attractive forces (Van de Waals etc.)
- Zeta potentially usually arises as polyelectrolyte dispersing agents are or ionic surfactants are adsorbed to particles
- These may also confer additional steric stabilisation
- Nanoparticles will require a **higher loading of dispersing agent to stabilize a suspension**



Nanoparticle Challenges: Safety

Solubility/dissolution and bioavailability

- Potential for nanoparticles to release an active ingredient more rapidly or at a higher dose, and hence have higher toxicity

Passing through barriers

- Smaller particles could potentially pass through skin and lung barriers into the bloodstream.
- High aspect ratio nano fibres/tubes could penetrate penetrate cells and cause damage (similar to asbestos)

Concerns expressed in e.g. food and cosmetics

- Legislation is now taking nano into account (e.g. EU regulations)

Nanotechnology in Agrochemicals

Potential benefits

- Increased rate of dissolution of hydrophobic AIs in spray tank or on crops
- Better distribution and retention of AI particles on crops
- Enhanced biological activity
- Increased rain-fastness
- Better targeting of pesticides on crops

→ Potential reduction in AI dosage and residues for same effect

Nanotechnology in Agrochemicals

Main categories:

- Used for enhanced solubility and bioavailability:
  - Micro-emulsion (ME) – particle size 6-50nm
  - Nano-emulsion – particle size 20-200nm
  - Nano-dispersion – particle size 50-200nm

- Used for targeted release and protection of the active ingredients:
  - Polymer based soft matrix – particle size 10-300nm
  - Solid lipid soft matrix – particle size 200nm-100µm – e.g. liposomes
  - Porous hollow silica hard matrix – particle size 100-200nm
  - Layered double hydroxides and clays (hard matrix) - µm range particle size
  - Nanosized metal or oxide particles combined with another active - µm range particle size
  - Nanosized metal or oxide particles alone – particle size 1-30nm

Critical Reviews in Environmental Science and Technology, 43: 1823–1867, 2013 and Frontiers in Chemistry 2015; 3: 64.

Nanotechnology in Agrochemicals

Sub-categories – polymer-based nanoformulations:

- Systems designed to control release and efficacy of the active ingredient;
- Greener nanopesticide formulations using biodegradable polymers or naturally derive active ingredients, for instance via:
  - Nanospheres - e.g. a polymer formulation of the biopesticide lansiumamide B showed improved efficacy;
  - Nanogels – e.g. a nanogel formulation was used to immobilize and control the release of pheromones and thereby reduce losses due to evaporation;
  - Electrospun nanofibres – e.g. fibres produced from poly(lactic) acid and cellulose have been used to formulate the insecticide thiomethoxam.
- Focus on polymers which can be destroyed by UV or biodegraded
  - E.g. lignin-polyethylene glycol-ethylcellulose, chitosan, alginate-bentonite and carboxymethyl chitosan-ricinoleic acid as well as many synthetic types

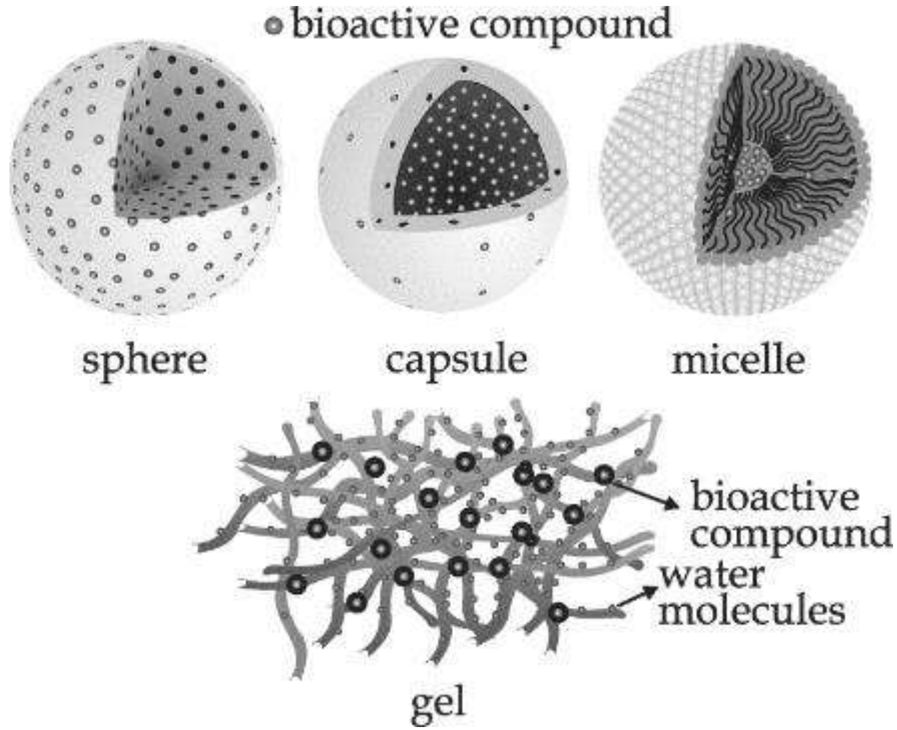
Environment International 63 (2014) 224–235.

Also http://www.intechopen.com/books/insecticides-development-of-safer-and-more-effective-technologies/polymeric-nanoparticle-based-insecticides-a-controlled-release-purpose-for-agrochemicals

Nanotechnology in Agrochemicals

Categories of controlled release nanoformulations

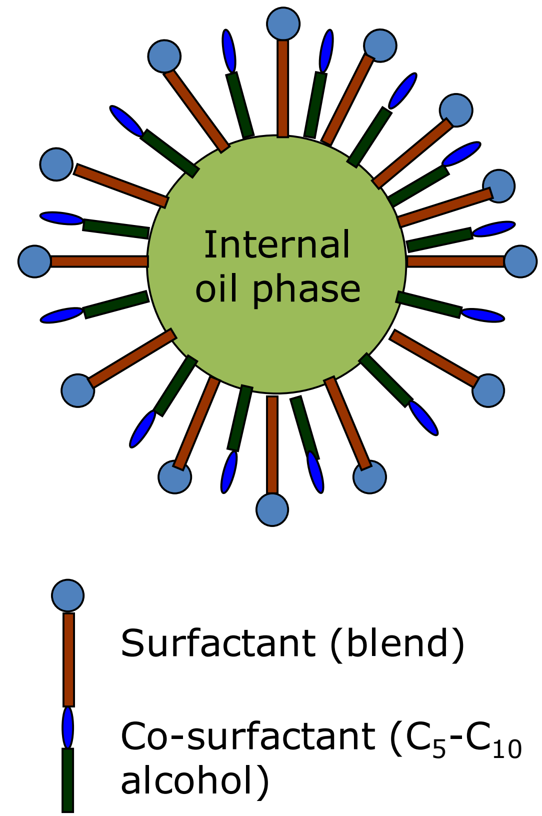
- Nanospheres: The active ingredient is distributed homogeneously in a polymeric matrix;
- Nanocapsules: The active ingredient is in the core of the particle, inside a polymeric shell;
- Nanogels: These are hydrophilic polymers which can absorb water as well as trap the active ingredient;
- Micelles: These spherical structures are formed when surfactants self-assemble in aqueous solutions and may trap active ingredient within them.



Taken from Bruno Perlatti et al "Polymeric Nanoparticle-Based Insecticides: A Controlled Release Purpose for Agrochemicals, Insecticides", InTech, DOI: 10.5772/53355 under a Creative Commons Attribution 3.0 Unported license. Available from: http://www.intechopen.com/books/insecticides-development-of-safer-and-more-effective-technologies/polymeric-nanoparticle-based-insecticides-a-controlled-release-purpose-for-agrochemicals

Nanotechnology in Agrochemicals
In reality, Microemulsions (ME) are Nano

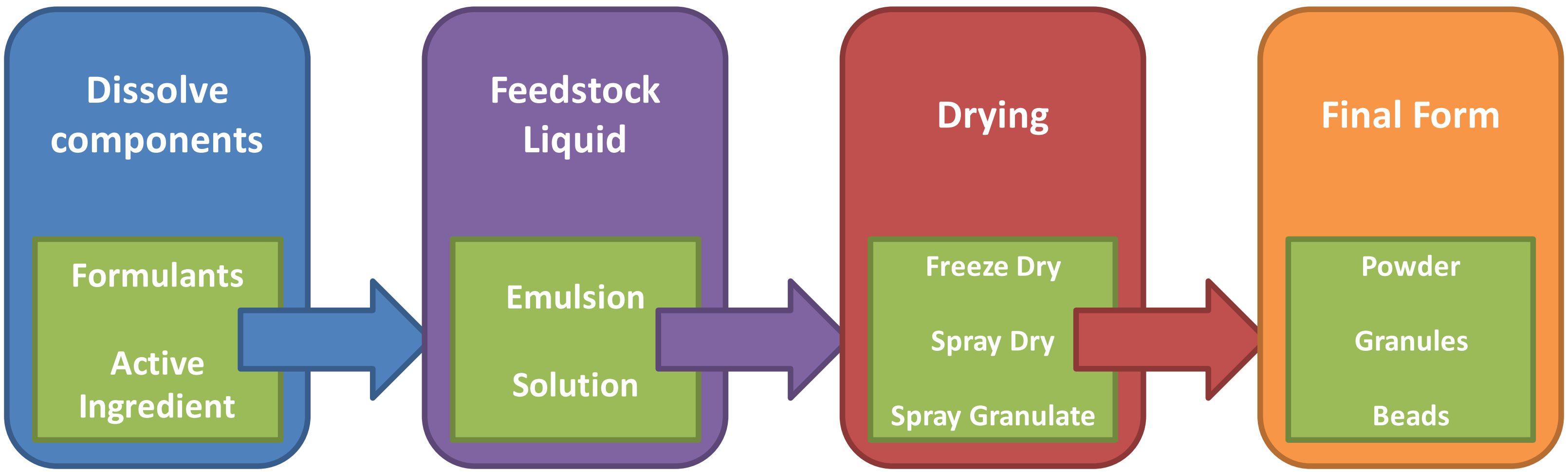
- ME have very fine droplets (10-50nm), so are in fact **nanosize** (not micro size), but ME are **not truly emulsions**
  - Transparent appearance
  - "Swollen micelle" structure - surfactant close-packing
  - Thermodynamically stable – Good shelf life
- Liquid AI (or AI in solvent) <30%, surfactant solubilisers, co-surfactant (e.g. medium chain length aliphatic alcohol), water.
  - Match hydrophobic part of solubilising surfactant with oil phase
  - Surfactant/alcohol combination gives extremely low oil/water interfacial tension and promotes formation of a microemulsion
- Easy water dilution, application. Potential for bioenhancement (penetration via surfactants)
- Blend AI and surfactants, make coarse o/w emulsion. Add co-surfactant and stir further.



Nanotechnology in Agrochemicals: Further Examples

Use of (micro)emulsion to template nanoparticles and then dry to form a solid dispersion

(Former Iota Nanosystems Ltd)

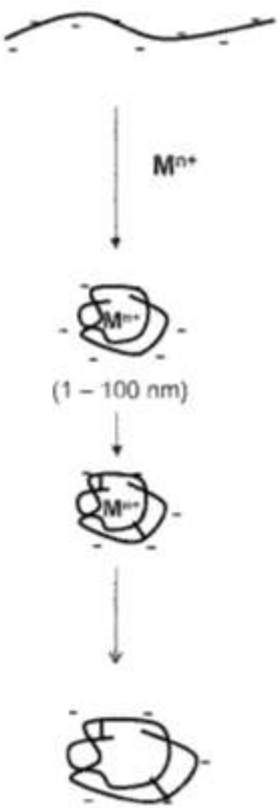


Adapted from http://www.specchemonline.com/featuredarticles/small-miracles
See e.g. Patent WO2012045994A1

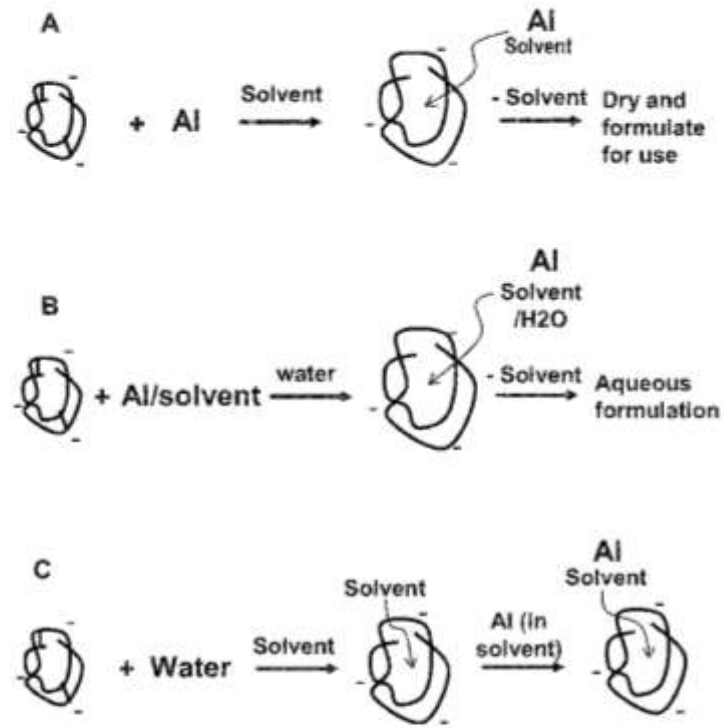
Some Commercial Examples

- Primo MAXX Plant Growth Regulator (Syngenta)
  - Said to be 100nm particle size nanoemulsion
- Banner MAXX fungicide (propiconazole – Syngenta)
  - Again said to be nanoemulsions
- Vive Allosperse – nanocages
  - "polymer particles…trademarked under the name Allosperse, which measure less than 10 nanometres in size...ultrasmall cages… which hold active pesticide ingredients and are engineered to disperse evenly in water"

Vive Allosperse – Nanocages – platform delivery technology

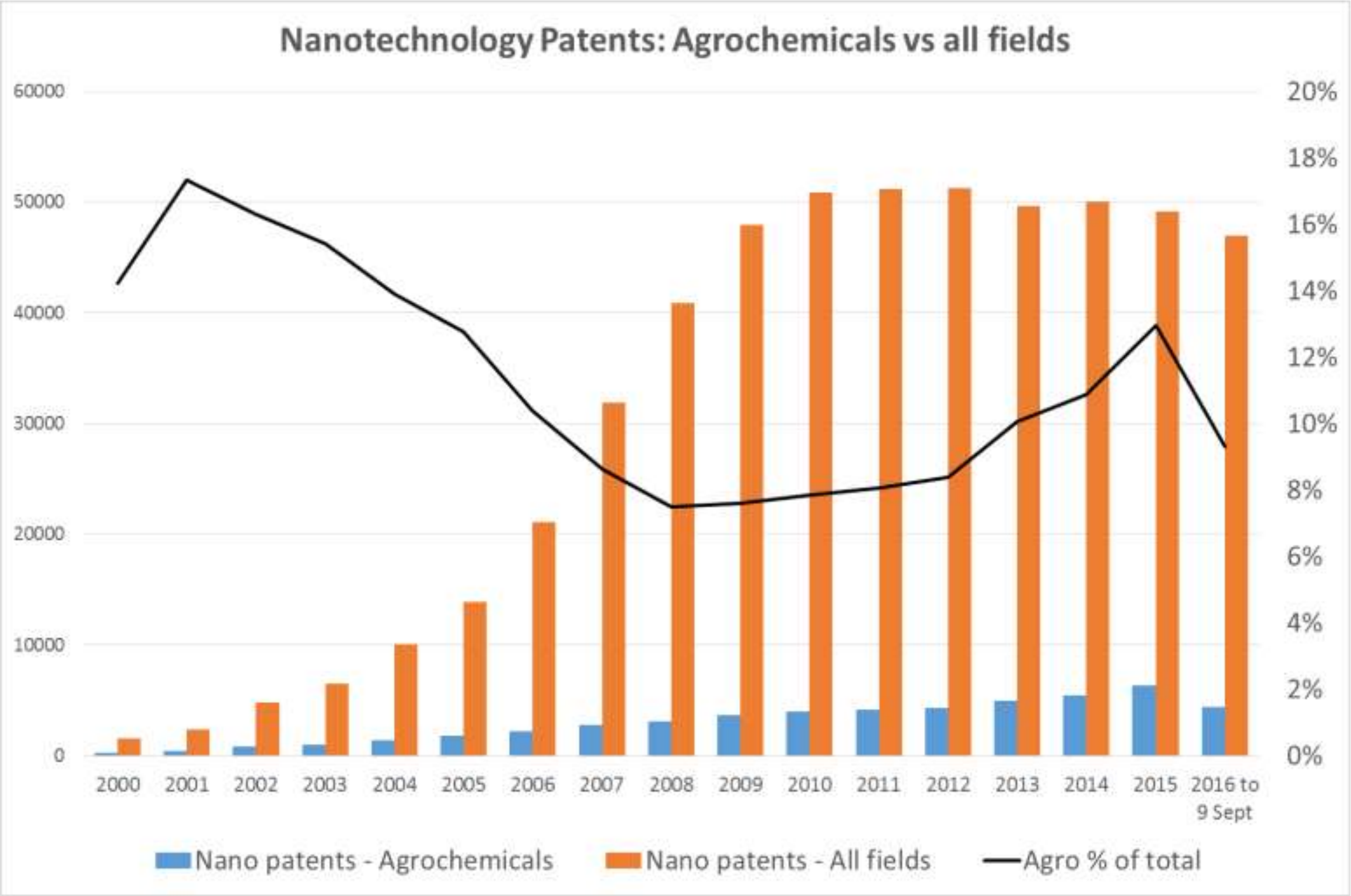


- Launched with azoxystrobin as AI in 2015
- Polymer based on chitosan and polyacrylic acid
- Dissolve negatively charged polymer in water. Repulsion causes polymers to spread out
- Add positive ions causing polymers to collapse in the form of a cage
- Deionise and add AI molecules which go to hydrophobic core of cage
- Outer shell of cage is hydrophilic and disperses in water
- After application and evaporation of spray droplet, AI migrates from cage
- L'Actualité chimique canadienne April 2012 http://www.vivecrop.com/ACCN_April2012.pdf



Patent US20130130904A1
See also http://vivecrop.com/technology/

Nanotechnology: The Plateau?



Agrow Formulations 2016. J.Bullock/D.Calvert, Informa Agribusiness Intelligence
https://store.agra-net.com/awfn16.html

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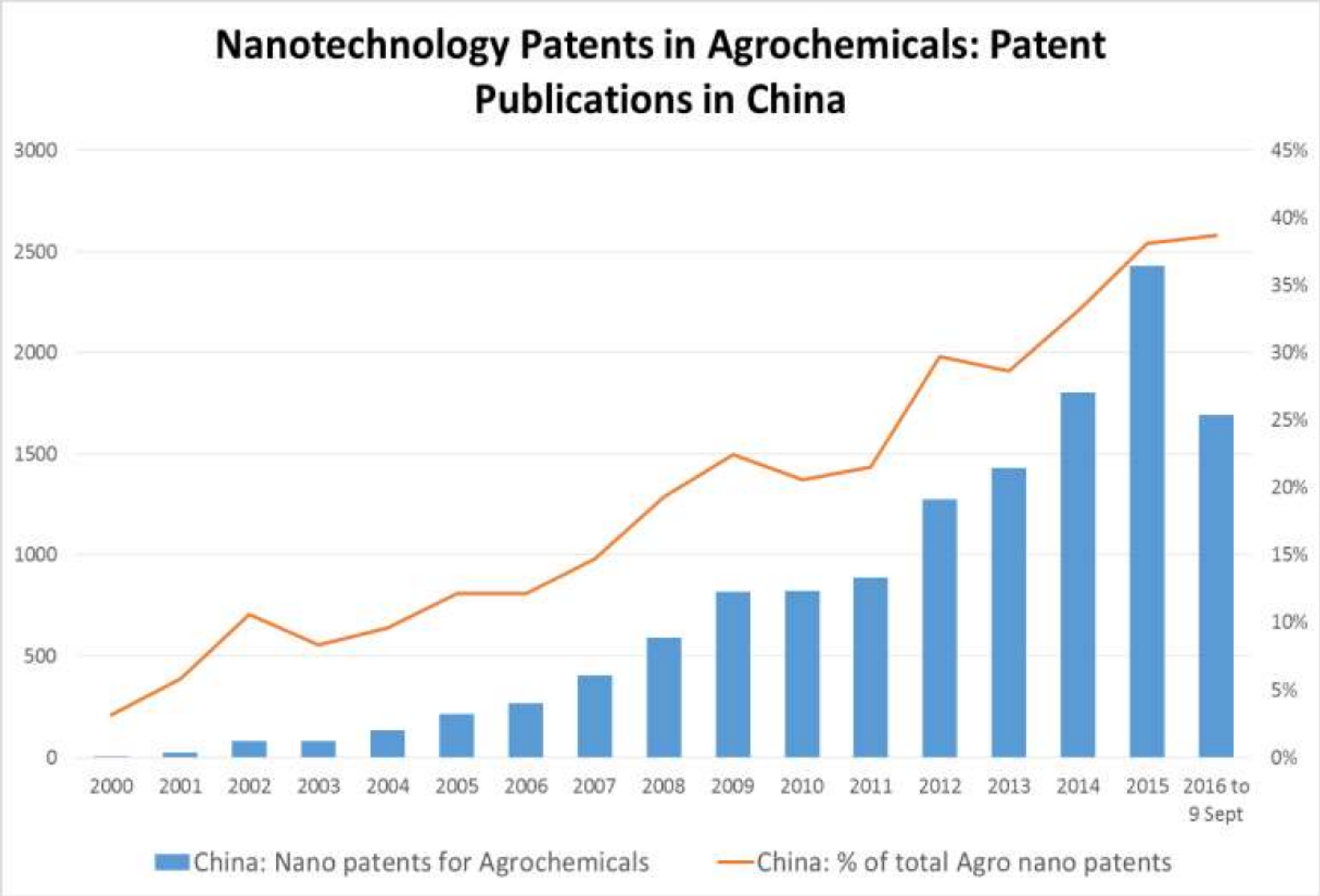
Who is Patenting Nano for Agrochemicals?



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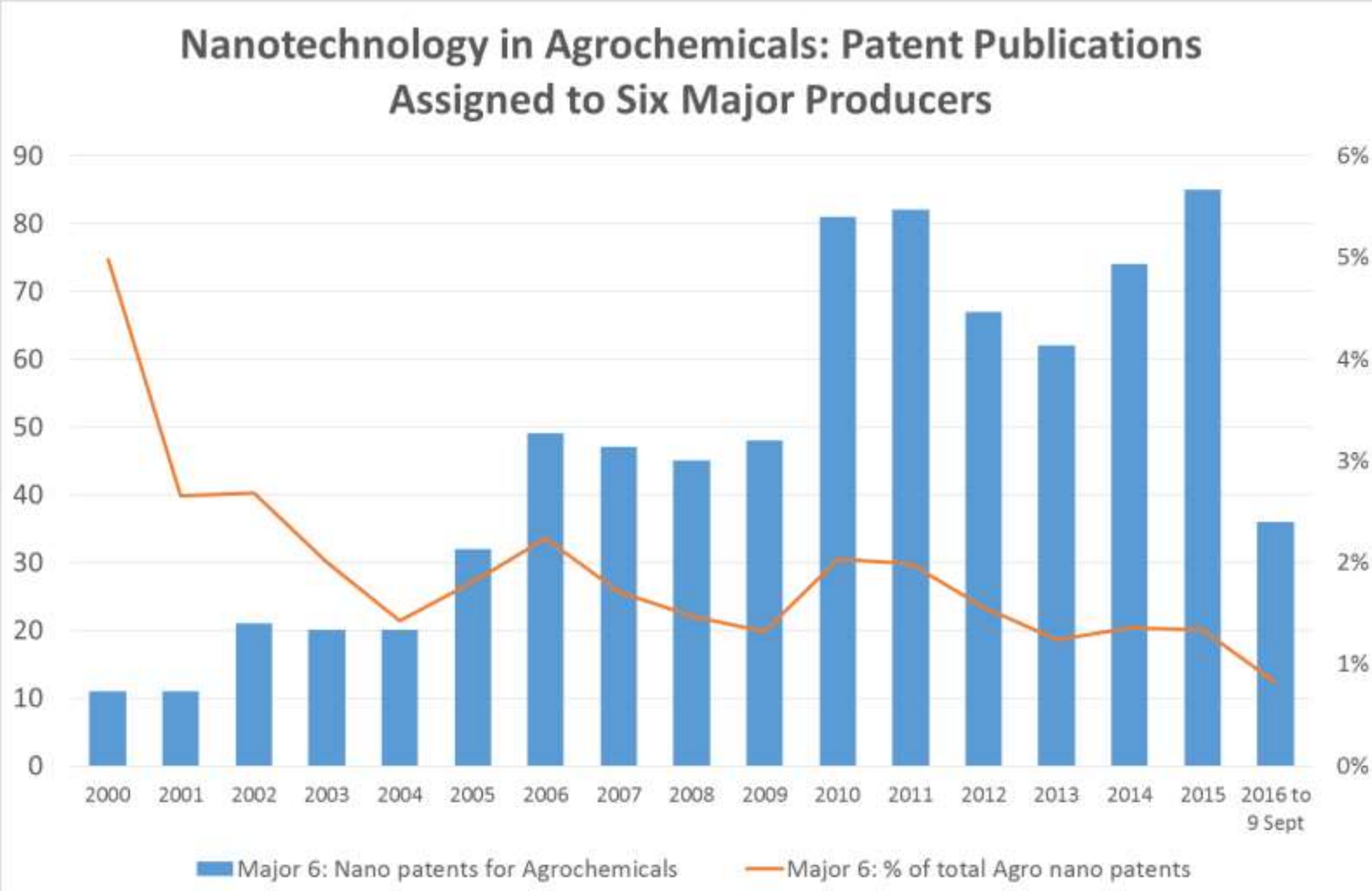
Who is Patenting Nano for Agrochemicals?



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Nanotechology: A Commercial Prospect – or not?

"There are over 3,000 patents worldwide for potential agrochemical usage of nanotechnology"

"However, **"in reality, today very few, if any**, intentionally manufactured nano-sized formulations exist on the market"

"Agrochemical large companies are constantly exploring the possibilities offered by nanotechnology, among other innovative technologies. However, at present, no significant data have been obtained in the development and impact of these products. **Nanotechnology is not seen by agrochemical industry as a technology that will have a major impact** on the crop protection industry in the foreseeable future and so far no agrochemical product is intentionally manufactured as a nanomaterial by these companies."

EU JRC Scientific and Policy Reports, Claudia Parisi, Mauro Vigani and Emilio Rodríguez-Cerezo, ISBN 978-92-79-37917-8 via https://ec.europa.eu/jrc/sites/default/files/ipts_jrc_89736_(online)__final.pdf

Despite numerous publications on potential safety issues and novel particles, our survey of launches and announcements confirms this position.

Conclusions and Discussion Points

- Nanotechnology can bring real benefits for agrochemicals
- There is high activity in publications and patents, especially, recently, in China
- The number of (openly announced) products on the market is relatively small
  - Costs still outweighing benefits?
  - Only use as an occasional problem solver?
  - Concerns about the "nano brand"?
- Possible discussion points
  - What is your experience?
  - Is it too complex/costly?
  - Is there really a need?
  - Would you use "nano" on your product literature?