

# New Trends in Chemistry of Magnetic Colloids: Polar and Non Polar Magnetic Fluids, Emulsions, Capsules and Vesicles

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Chemical synthesis of charged magnetic nanoparticles (spinel ferrite type) dispersed in water allows the production of ionic ferrofluids. These charges, which are beared by hydroxyl groups linked with surface iron atoms, are used to adsorb several types of ions or molecules on the particles. Adsorption is performed either through electrostatic interactions between the surface charges and the charges of the adsorbing ions, or through chelation of the surface iron atoms by complexing molecules. Processes are described for adsorption of ionic species, of surfactant molecules and of polymeric chains. Coated or non coated particles are dispersed in polar or non polar media in order to form magnetic colloidal solutions. These solutions may themselves be a component of more complex magnetic systems. Synthesis of magnetic emulsions, magnetic capsules and magnetic vesicles are described. The choice of the particle coatings (sign and nature of charges, nature of the surfactant or polymeric chains adsorbed) is the most important point for the successful synthesis of such complex magnetic colloids.

## I - Introduction

Ferrofluids are colloidal suspensions of finely divided magnetic particles<sup>[1]</sup>. The union of both fluid and magnetic properties leads already to numerous industrial applications and researchs in the area of physics and seems also to be full of promise in the biornedical field<sup>[2]</sup>.

The first ferrofluids were obtained by grinding magnetic materials in presence of solvent and surfactant<sup>[3,4]</sup>. The chemical synthesis, proposed by Khalafalla and Reimers in 1973<sup>[5]</sup>, allows the production of ferrofluids stabilized by the coating of the particles with oleic acid. Since these pioneering works, various other methods of preparation have been proposed<sup>[6-9]</sup>. For its part, the chemical process proposed by Massart in 1979<sup>[10]</sup>, leads to the synthesis, in aqueous media, of versatile products: the nanoscale magnetic particles have a very reactive surface allowing the stabilization of the particles in a large spectrum of media including both polar and non polar solvents. In order to realize each particular application, it is necessary to synthesize a particular ferrofluid well suited to its application. It is clear that the main difficulty is a good fitting of the particles with

the carrier medium. We present here a review, fifteen years after the first Massart's synthesis, of the state of the art of this process, distinguishing two main steps:

- 1 - Standardized synthesis of an aqueous precursory ferrofluid.
- 2 - Surface chemistry and peptization of the particles in the desired carrier.

In the first Section we review the general procedure of the chemical synthesis of the precursory ferrofluid which is characterized by a given particle size distribution and a given surface charge density for the particles dispersed in water. The second Section concerns the principles of the particles peptization in various media. In the last Section, we give several examples of ferrofluids used for specific microscopic applications as nanoscale probes or as part of a more complex magnetic medium.

## II. Precursory to ferrofluid synthesis. Size and charge of the particles

The initial Massart's process leads directly to the formation of stable aqueous sols constituted by charged

particles of maghemite peptized in acidic or alkaline media. Afterwards, this method has been extended to the synthesis of other types of ferrite  $Fe_2 MO_4$  sols:  $M = Co$  or  $Mn$ <sup>[11,12]</sup>  $M = Zn$ <sup>[13]</sup>. The ferrite particles are obtained by coprecipitation of a mixture of salts of divalent and ferric cations in alkaline medium. After washing, the particles are dispersed in acidic or in alkaline medium.

Oxidation of the magnetite at 100°C in an aqueous solution of ferric nitrate leads to maghemite particles ( $\gamma Fe_2O_3$ ) without noticeable modification of size characteristics<sup>[14]</sup>.

The synthesized particles, observed through transmission electron microscopy, appear roughly spherical. Samples are always polydisperse and a log-normal distribution  $P$  (Fig. 1) is assumed for the diameter  $D$  of the particles<sup>[15]</sup>:

$$P(D) = \frac{1}{D\sigma\sqrt{2\pi}} \exp \left[ -\frac{\ln^2(D/D_0)}{2\sigma^2} \right],$$

where  $\sigma$  is the standard deviation and  $D_0$  the mean value of  $D$ .

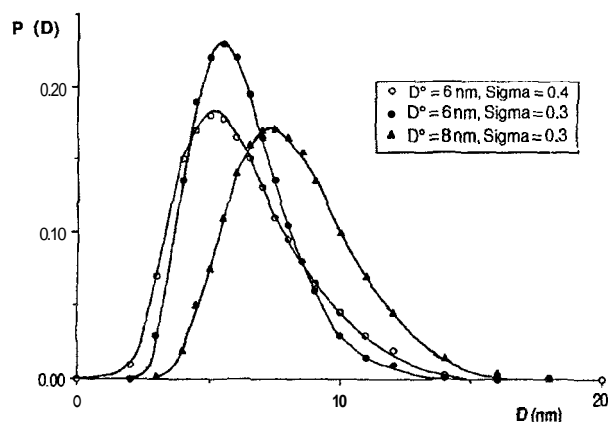


Figure 1: Example of size distribution of maghemite particles.

Particles size depends upon adjustable parameters of the coprecipitation step<sup>[16]</sup>:

- total concentration of cations ( $M^{2+} + Fe^{3+}$ )
- nature of the alkaline medium
- pH and temperature

Usually, the particles diameter that may be obtained by this procedure is in the range of 2 - 20 nm with  $D_0 \approx 7$  nm and  $\sigma \approx 0.35$ .

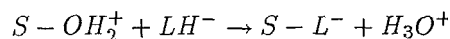
In aqueous media, the electric charges of the particles are due to the specific adsorption of amphoteric hydroxyl groups. The density of particles surface charge is a function of the pH of the medium<sup>[17,18]</sup>: the particles

are positively charged in acidic medium and negative in alkaline medium. The point of zero charge (PZC) is located at pH 7,5 and in the range of pH 6 - 10, the surface charge is too small to permit the peptization of the particles. In alkaline medium, the particles can be dispersed or not according to the nature of the counterion. A stable ferrofluid is obtained in presence of counterions like  $TMA^+$  (tetramethylammonium cation) but with more polarizing cations ( $Na^+$ ,  $NH_4^+$ ), the particles flocculate. In the same way, in acidic medium, stable precursory ferrofluid can be obtained with suitable counterions like  $NO_3^-$  or  $ClO_4^-$ .

### III. Fitting and peptization of the particles in aqueous or non polar media

#### 1. Aqueous media

The aqueous precursory ferrofluids are very sensitive to the pH and their use is limited ( $pH < 6$  or  $pH > 10$ ). It is possible to replace the surface amphoteric hydroxyl group (or its protonated form  $-OH_2^+$  in acidic medium) by chelating agents (for instance, an anionic ligand  $LH^-$ ):



When the particles are coated by  $LH^-$ , the PZC is shifted to lower pH. For example, with the citrate ligand, the PZC drops to pH 2 and particles are peptizable at  $pH > 4$ <sup>[19]</sup>.

Nevertheless, complexing agents can be reducing agents (ascorbic, oxalic or salicylic acids). The reduction of surface ferric cations leads to the decomposition of the particles. We have checked the chemical stability of the maghemite particles coated by a lot of chelating agents; the best ones we found are the  $\alpha$  - hydroxy acids (citric, tartaric, malic and tartronic acids) which contain the chelating group  $CHOH - COOH$  and supplementary carboxylate groups which ensure the surface negative charge density of the particles. Also dimer-captosuccinic acid<sup>[20]</sup>, by the  $-CHSH -COOH$  group, is a good chelating agent and leads to stable ferrofluids in biological media.

#### b. Non polar media

It is well known that peptization of magnetic particles in non polar media is possible only if their surface

has a good affinity with the solvent molecules. It is not the case for the charged particles of the precursory ferrofluid. So, it is necessary to coat them with surfactant molecules (Fig. 2). With particles positively charged of acidic precursor, we commonly use oleate, sodium dodecylsulfate  $\text{CH}_3 - (\text{CH}_2)_{11} - \text{OSO}_3^-$  (SDS) or Beycostat NE (BNE) which is an industrial complex mixture containing mono- and diester phosphates (Gerland S.A.). With particles negatively charged of alkaline precursor, we mainly use EMCOL CC 59 which is an industrial surfactant (WITCOT SA) containing cationic quaternary amine group.

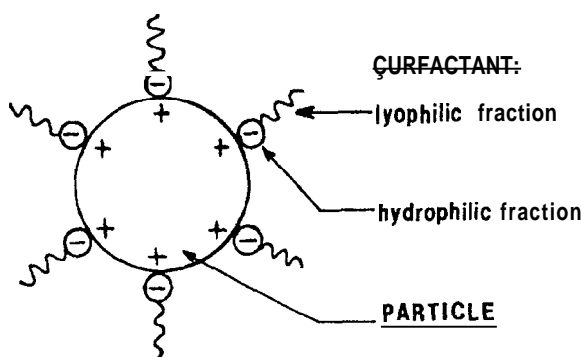


Figure 2: Coating of charged particles by surfactants.

The hydrophobic part of the surfactant must have a good affinity with the solvent in order to permit the peptization of the particles. Table 1 displays the different kinds of surfactants and washing agents used according to the solvent<sup>[21]</sup>. The choice of the surfactant in order to obtain a stable sol is still empirical.

The synthesis of ferrofluids in non polar media proceeds in three steps:

1 - Flocculation of the precursory ferrofluid in aqueous medium by charge compensation with the surfactant whose tail is chosen so as to have the same structure than the solvent

2 - Washing of the flocculate with alcohol in order to eliminate the residual water (replaced by ether in the use of EMCOL CC 59 because this latter is strongly soluble in methanol).

3 - Peptization of the particles coated with the surfactant into the organic medium.

In special media it can be necessary to add a "co-

surfactant" to obtain a better affinity between the particles and the solvent<sup>[18]</sup>.

Special cases of surfactants are those constituted by a polymeric chain (for example, a polystyrene or a polymethylmetacrylate chain) functionalized at one end by a sulfonate group for example<sup>[22]</sup>:

Maghemite particles have been coated by such polystyrene chains ( $M = 13,000$ ) and then, dispersed in cyclohexane. Viscosity measurements (Einstein's law) have shown that the average hydrodynamic diameter of the particles was greater than in the case of particles coated by small surfactant molecules, allowing to estimate the thickness of the coat as 8 nm.

#### IV. Examples of ferrofluids for particular microscopic applications

Magnetic fluids have many industrial applications. It is not our purpose to discuss this point. The applications of magnetic ferrofluids that we shall present below are some "applications for research" in other fields as Physics, Chemical Physics and Biology.

##### 1. Linkage antibody - magnetic particles for biomedical applications<sup>[20]</sup>

For many biomedical applications it is necessary to link magnetic particles to a cell. This cell targeting can be ensured by interaction between an antigen, located on the cell membrane, and a specific antibody linked to the particle. With this aim, we have used 7B10 antibody, of IgG type, raised against an antigen of human breast cancer cells<sup>[23]</sup>.

The linkage between the antibody and the particle must respect three laws:

- The linkage must be strong.
- The antibody - particle conjugates must be peptizable in biological medium.
- The immune specificity of the antibody must be preserved.

For these reasons we have proceeded in three steps (Fig. 3):

SOLVENT	SURFACTANT	WASHING PROCESS
Alkanes	SDS or Oleic Acid	Methanol
Alcohol	EMCOL CC 59	Ether
Acetone	BNE	Methanol
Ethyl Acetate	BNE + Pentanol 1	Methanol
Benzene	BNE	Methanol
Camphene	BNE	Ethanol
Chloroform	BNE	Methanol
Cyclohexane	BNE or Oleic Acid	Methanol
Ether	BNE	Methanol
Dibutylphthalate	BNE	Ethanol
Dichloromethane	BNE	Methanol
Oil	BNE	Ethanol
Methyl Ethyl Ketone	BNE	Methanol
Resin	Oleic Acid	Ethanol
Styrene	BNE	Methanol
Carbon Tetrachloride	BNE	Methanol
Tetrahydrofuran	BNE	Methanol
Toluene	BNE	Methanol
Xylene	BNE	Methanol

Table 1: Which surfactant for which solvent? from Ref. [21]

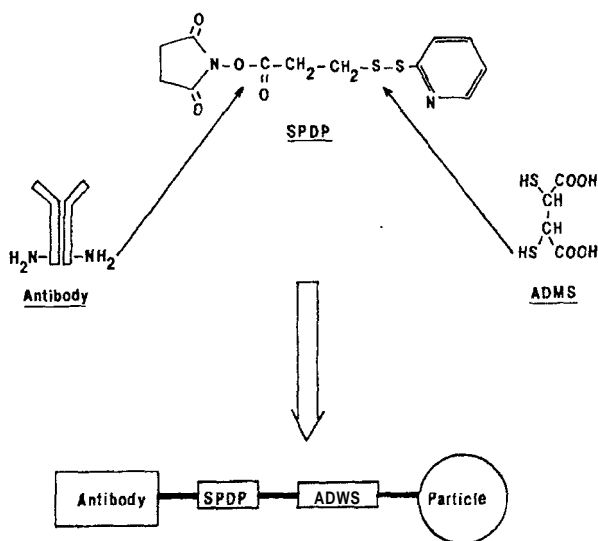


Figure 3: Linkage antibody - magnetic particles.

1 - Linkage of the antibody with an intermediary molecule SPDP (N-succinimidyl 3-(2-pyridyldithio)propionate). A peptide bond is formed between a carboxylate group of SPDP and amine groups of the antibody. These amine groups are located in the constant fraction of the antibody which is not involved in the immune properties<sup>[24]</sup>.

2 - Complexation of the maghemite particles of the acidic precursor with ADMS (dimercaptosuccinic acid).

3 - Covalent S-S bridge formation between ADMS (with its second thiol group) and SPDP (with its sulfur atom).

The linkage of maghemite particles coated by the 7B10 antibody with the membrane of human breast cancer cells has been demonstrated by immunofluorescence tests and by transmission electron microscopy.

## 2. Magnetic particles of ferrofluids as viscosity probes during sol-gel processes<sup>[25]</sup>

It is well known that magnetic solutions become birefringent when they are submitted to a magnetic field. Although the microscopic origin of this phenomenon is not clearly established, it depends on the physical alignment of particles along the field. Thus, when the field is switched off, particles relax and the birefringence signal decreases with a characteristic time which is function of the particle size and of the viscosity of the medium. Sol-gel transitions can be studied taking advantage of this property, using ferrofluid particles as magnetic probes, dispersed in the carrier medium<sup>[26]</sup>.

For example, ferrofluids have been used to study the alumino-silicate gels formation in water-isopropyl alcohol mixture. In order to obtain stable sols in this medium, the maghemite particles have been coated according to the double mechanism:

1 - Chelation of the particles of acidic precursory ferrofluid with citrate.

2 - Coating of the negative complexed particles with the EMCOL CC 59 cationic surfactant.

3. Ferrofluids in magnetic emulsions and capsules

a. Magnetic emulsions

Magnetic emulsions have been considered by several authors<sup>[27]</sup>. They are suspensions of droplets of ferrofluid dispersed in an immiscible phase. The emulsion may be an oily magnetic fluid in water or an aqueous magnetic fluid in an organic phase. The size of the droplets is in the range of 0,1 - 10  $\mu$ m.

Fig. 4a is a schema of an emulsion constituted by an oily magnetic fluid dispersed in water<sup>[28,29]</sup>.  $\text{CoFe}_2\text{O}_4$  particles coated by BeycoStat NE are dispersed in oil. The interface oil/water of the emulsion is ensured by another tensioactive SDS (sodium dodecylsulfate).

Fig. 4b is a schema of an emulsion constituted by an aqueous magnetic fluid (maghemite particles in acidic medium) dispersed in an ether- cyclohexane mixture<sup>[30]</sup>. The interface between aqueous and organic phases is ensured by DDAB (didodecyl-dimethylammonium bromide) which is a double chain cationic surfactant (DDAB does not adsorb on the particles).

b. Magnetic microcapsules<sup>[21-28,29]</sup>

For some applications, it is necessary to rigidify the interface oil/water using specific surface agent or making interface polymerisation. So the oily droplets become microcapsules.

The polymerization of the interface can be performed according to different procedures. For example (Fig. 5), the oily ferrofluid is dispersed in an alkaline aqueous medium which contains maleic ethyl anhydrid. This latter is a copolymer which precipitates at the interface when the pH is decreased. After heating in presence of melamine-formol resin, the chains of precipitated copolymer are linked. The pH is then adjusted to 7.

The size of the spherical capsules, observed by optical microscopy, is in the range of 1 - 10  $\mu$ m.

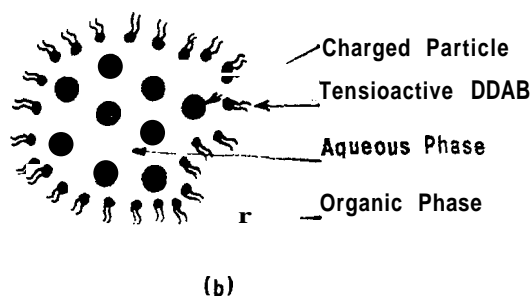
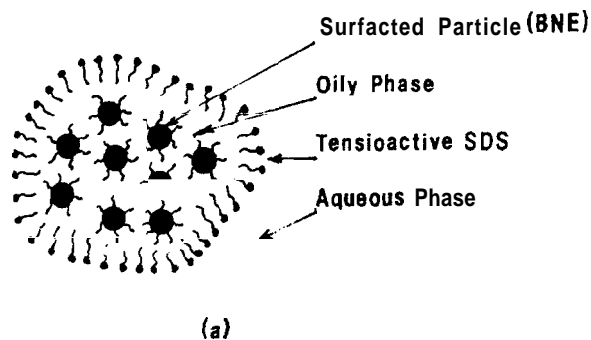


Figure 4: Magnetic emulsions.

4. Ferrofluids in vesicles and liposomes: a tool to measure bending modulus of bilayers

Magnetic vesicles constitute an useful model for the research in different areas such as Physics and Biochemistry.

One of the main difficulty of the synthesis is to confine the ferrofluid only in the aqueous phase entrapped in the vesicle. With this aim, an original procedure has been developed (Fig. 6):

A "double emulsion" is formed: an aqueous magnetic fluid is dispersed in a low boiling point solvent. The emulsion is then dispersed again in water. The tensioactive agent ensuring the both interfaces is the tensioactive forming the bilayer. By evaporation of the intermediary organic phase, both tensioactive layers join themselves side by side and constitute the vesicle double layer.

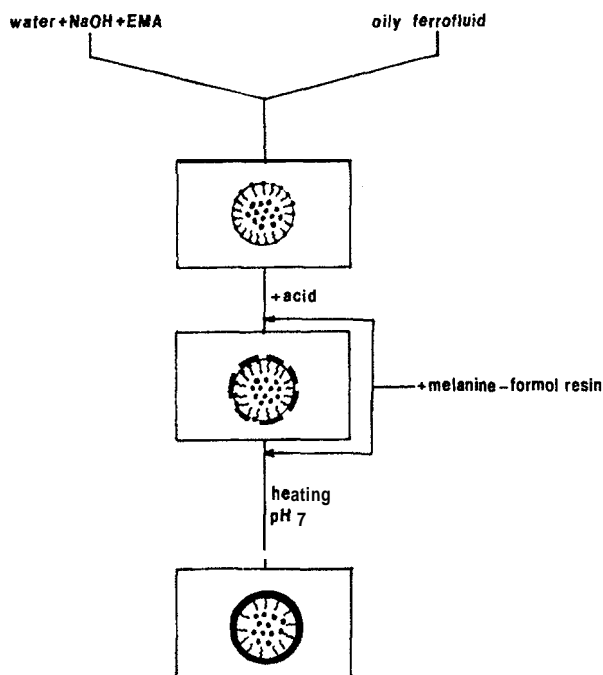


Figure 5: Magnetic microcapsules synthesis<sup>[15]</sup>.

It is possible, by this procedure, to obtain magnetic vesicles with DDAB bilayers<sup>[30]</sup> or with phospholipides bilayers<sup>[31]</sup>. In this last case, some liposomes are flaccid and elongate when a magnetic field is applied, the elongation being correlated to the bending modulus of the membrane<sup>[32]</sup>

d. **Ferrofluids** in bidimensional colloids<sup>[33]</sup>

Cyclohexane magnetic fluids, constituted by Beycostat NE coated particles, have successfully replaced cyclohexane in the polyphasic system water, cyclohexane, SDS, pentanol, in order to obtain lamellar phases which are constituted by a periodic packing of a lamellar aqueous phase alternating with a cyclohexane one. In the present case, particles stay confined in the cyclohexane lamellar and the so called "ferrosmectic" phases are obtained.

The mean thickness of lamella is 4 nm for the aqueous phase and in the range of 10 - 40 nm for the organic phase (Fig. 7).

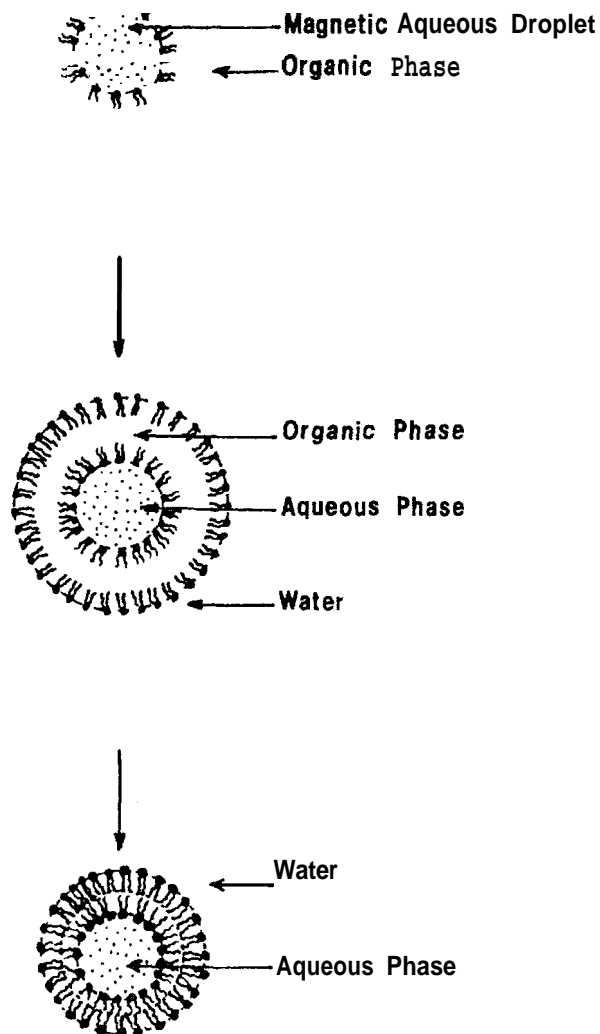


Figure 6: Magnetic vesicles synthesis.

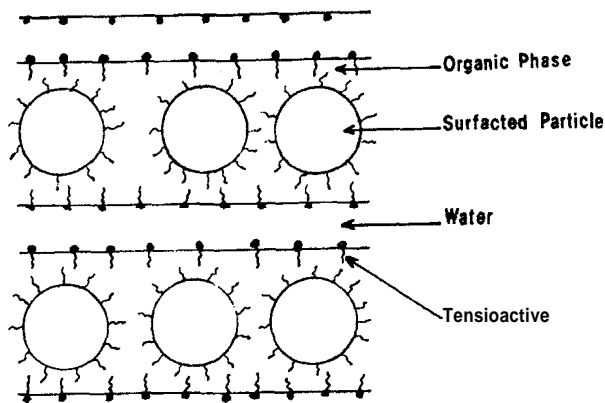


Figure 7: Ferrosmectic phases.

Such systems offer a large domain of investigation both as special bidimensional ferrofluid and as an ex-

ample of the compatibility between solid particles and structured liquids.

## V. Conclusion

In view of the permanent extension of the ferrofluid use in both theoretical research and industrial applications area, the chemist is able to synthesize specific products. The large variety of surfactants and chelating agents permits to fit the particle surface with the dispersion medium.

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