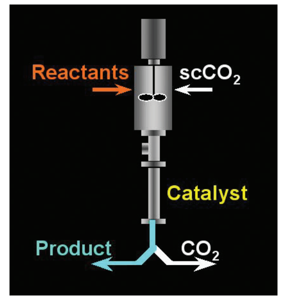
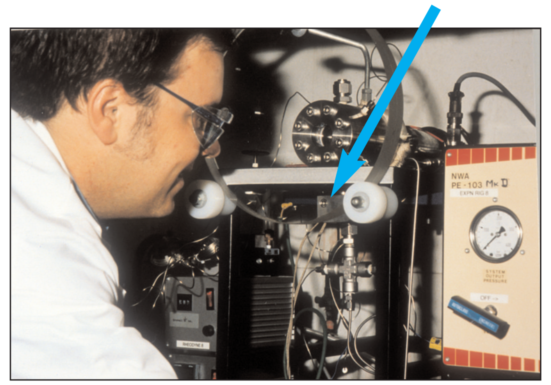
## *Reactions in SCFs*

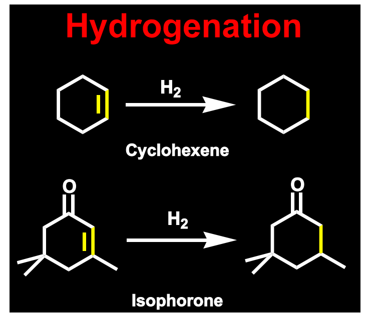
**SCFs offer chemists greater control over reaction chemistry. Reactions involving hydrogen ($H_2$) are particularly effective because $scCO_2$ allows $H_2$ to be mixed very efficiently with the other reactants. Toxic solvents can be avoided, equipment can be made smaller and unwanted side-products eliminated.**



Most chemical reactions require a solvent, to aid mixing, remove heat and consequently control reactivity. Many traditional solvents are toxic or environmentally damaging, as a result their disposal is often very costly. Our research group is particularly interested in replacing organic solvents in chemical reactions. Our strategy is to demonstrate that SCF solvent systems can give real chemical advantage as well as being environmentally more acceptable.



We have developed a versatile SCF reactor system, as part of a thriving collaboration with the fine chemicals company Thomas Swan & Co Ltd. Our flow reactor system is extremely safe and very simple. As you can see in the photograph, the apparatus is surprisingly small but it can still produce literally tons of product per year.



"Hydrogenation", or the addition of $H_2$ to an organic compound is a fundamental industrial process that is carried out daily on a multi-ton scale. Supercritical hydrogenation has been shown to be very efficient; furthermore the selectivity of supercritical hydrogenations can be controlled with high precision because the reaction conditions employed (temperature, pressure and reactant concentration) can be adjusted more or less independently of one another.

The combination of $scCO_2$, solid catalyst and flow reactor is extremely efficient. The photograph shows the metal reactor tube with a beaker of catalyst. In only two minutes, this amount of catalyst can hydrogenate all of the liquid (cyclohexene) in the two glass cylinders. In another reaction, the hydrogenation of isophorone, 1 gram of catalyst can hydrogenate as much as 7.5 kilos of isophorone before losing its activity.

Although $CO_2$ has been identified as a primary greenhouse gas, the gas that we use is the waste product from other industrial processes, such as ammonia production. Therefore, we are not increasing the amount of $CO_2$ produced.

**In 2002, Thomas Swan and Co. Ltd. opened a full-size plant based on our work that can produce 1000 tons of material per year. The plant is highly flexible; change the catalyst and you change the chemistry.**

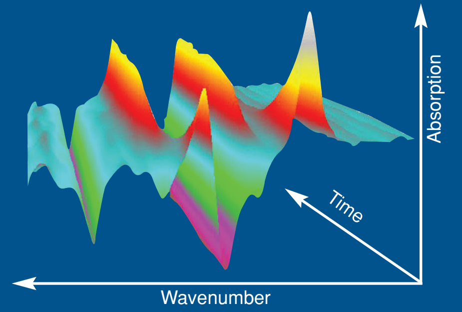
For more information on chemical reactions in SCFs, see:-

- Oakes, R. S., Clifford, A. A. & Rayner, C. M. "The use of supercritical fluids in synthetic organic chemistry" *J. Chemical Society-Perkin Transactions 1*, 917-941 (2001).
- Hyde, J. R., Licence, P., Carter, D. N., & Poliakoff, M. "Continuous catalytic reactions in supercritical fluids" *Applied Catalysis A: General* **222**, 119-131 (2001).

## *Mechanisms of Reactions in Supercritical Fluids*

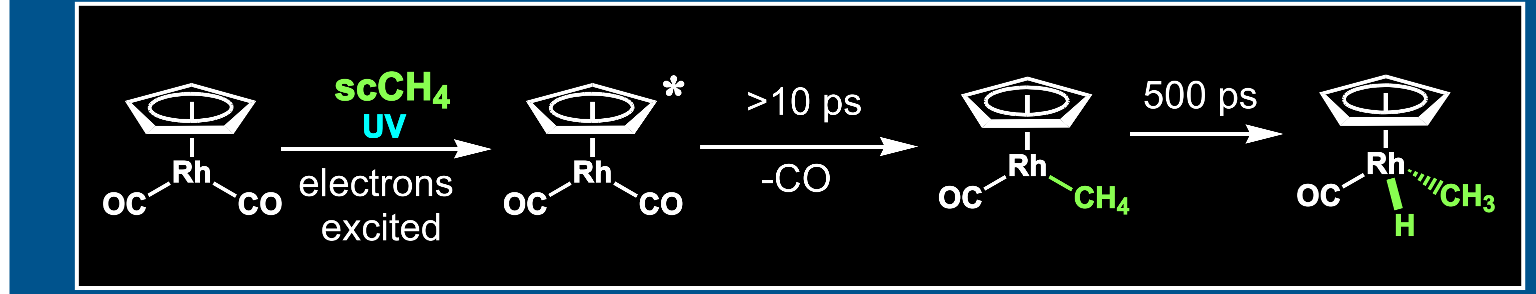
**Even quite simple chemical reactions can have quite complicated mechanisms. Using fast infrared spectroscopy, we can fingerprint short-lived molecules that are formed in the course of chemical reactions. Supercritical fluids give these measurements an added dimension since you can vary density and other properties over a wide range.**

Infrared spectroscopy provides a very characteristic fingerprint for most molecules. With the correct apparatus, the spectra can be recorded very rapidly in a millionth of a second (microsecond) or even with highly sophisticated equipment on the timescale of a billionth of a second (picosecond). This allows us to detect compounds which are formed one after another in the course of a chemical reaction. If you can detect these, you can learn about how chemical reactions occur. The chemists in the photo are using the Time - Resolved IR apparatus at Nottingham.



We can now carry out these measurements in SCFs which are becoming increasingly recognized as solvents for chemical reactions. However, a key scientific question is precisely how these unique fluids affect chemical reactions. Fast infared spectroscopy is beginning to provide the answer.

Our team has led the development of a national facility (***PIRATE***) for picosecond infrared measurements at the Rutherford Appleton Laboratory, Oxford. For example, the reaction of metal compounds with methane is of industrial interest. We have shown that the reaction of a rhodium complex in supercritical methane ($CH_4$) takes place in three stages: (1) excitation of the molecule, (2) bonding of the $CH_4$ to the Rh atom and finally (3) breaking of the C-H bond. The whole reaction is complete in 500 ps (5x$10^{-10}$ seconds).



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# Supercritical Fluids:
# Clean Solvents
# for Green Chemistry

What happens when a liquid is heated in a sealed container?

you create a fluid with most unusual properties

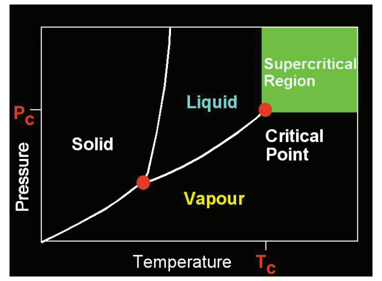
## THE CLEAN TECHNOLOGY GROUP

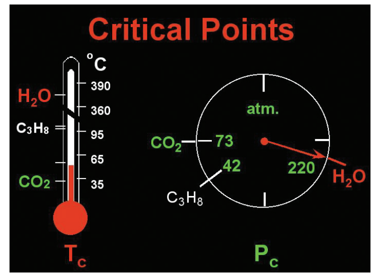
The School of Chemistry, The University of Nottingham.

# *What are Supercritical Fluids (SCFs)?*

**SCFs are gases compressed until they are nearly as dense as a liquid. Like gases, SCFs are highly compressible and must be contained in closed vessel. Like liquids, SCFs can dissolve solid materials.**

For nearly 200 years, scientists have been fascinated by watching liquids being heated in sealed tubes. The photograph shows what happens; the liquid has been coloured with blue dye so that it shows up more clearly. When the liquid is heated, it expands and some of it evaporates. This makes the vapour above the liquid grow denser. Eventually, the vapour and liquid reach the same density and the meniscus between them becomes blurred and disappears. The liquid has become “Supercritical”. (Warning: this experiment involves high pressures and you should never try to do it yourself, except at the Science Museum, London).

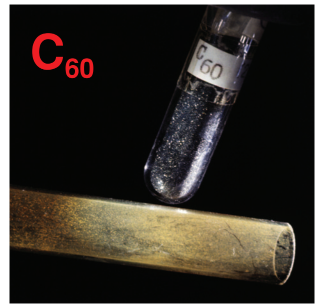


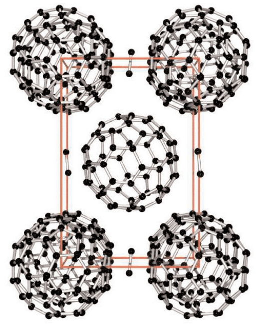


Chemists describe this behaviour with a phase diagram, a plot of the Pressure against Temperature. The point where the boundary between gas and liquid disappears is called the Critical Point. A fluid is “Supercritical” when its temperature and pressure are above their critical values, $T_c$ and $P_c$.

Supercritical $CO_2$ ($scCO_2$) is the most widely studied SCF. It is non-toxic and $T_c$ is close to room temperature; this means that it can be used with delicate materials, such as enzymes, which would be damaged by higher temperatures (see next pages). Chemists are beginning to use $scCO_2$ as a replacement for environmentally less acceptable solvents. $scCO_2$ has been exploited commercially to decaffeinate coffee for several years.

caffeine





$scCO_2$ cannot dissolve larger molecules but it can be mixed with ordinary solutions of these molecules to cause precipitation. By carefully selecting the conditions, you can control this precipitation to leave particles of just the size you want. For example we have controlled the precipitation of $C_{60}$ (Buckminsterfullerene) to make new materials that contain gas molecules trapped between the $C_{60}$“footballs”. Depending on the conditions, we can make anything from a finely divided yellow powder (500 nm) to larger crystals (1 mm) that are black.

## *SCFs are not new!*

The first scientist to heat a liquid in a sealed tube or at least to survive such an experiment was Baron Cagniard de la Tour (*Ann. Chim. Phys.* 1822, **21**, 127-132). The term “critical point” was coined by Thomas Andrews in the mid-nineteenth century who worked at Queen’s University, Belfast. (*Phil. Trans. Roy. Soc.* 1869, **159**, 575-590).

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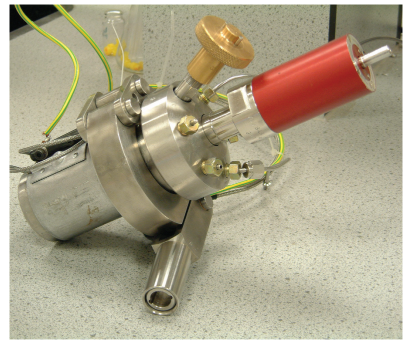
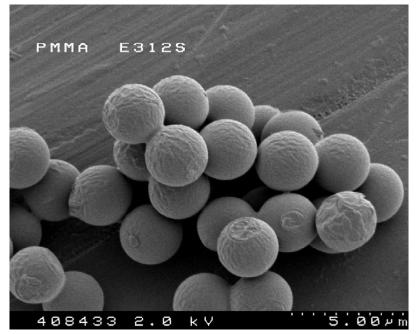
# *Polymers and SCFs*

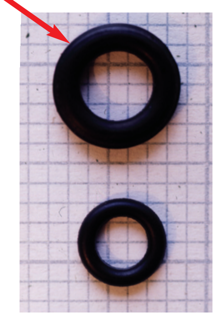
**Polymers (plastics) are important in a whole range of industries. $scCO_2$ can make the production of polymers cleaner and often gives greater control than conventional processing, leading to new and better products.**

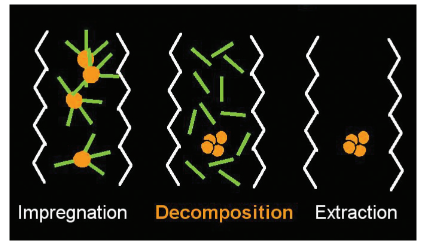


Several research groups, including Nottingham, are using $scCO_2$ as a solvent for making polymers. The reactions are carried out in a high-pressure vessel, about the size of a coffee mug. The polymer comes out of the reaction as uniform particles, which are “clean and dry”. The only residue is $CO_2$ which quickly diffuses away.

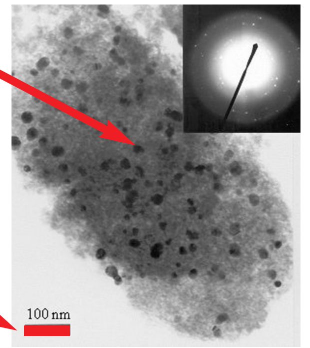


SCFs are gas-like. They penetrate and swell many polymers very effectively. The picture shows two identical “O-rings”. The one at the top has been exposed to $scCO_2$ and has swollen to twice its normal size! It takes about 20 minutes for the $CO_2$ to come out and for the O-ring to shrink back to normal. You can see the $CO_2$ bubbling out if you drop the swollen ring into lime water ($CO_2$ turns the lime water milky).



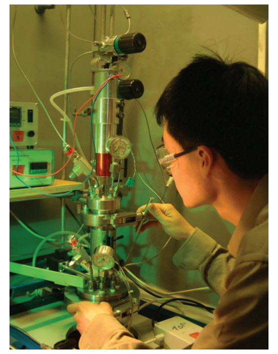


We have used this swelling to load tiny “nanoparticles” of silver metal into polymers. The route involves dissolving a silver containing compound in $scCO_2$ and then supercritically dyeing the polymer (impregnation). Then, the compound is carefully decomposed releasing the desired silver nanoparticles, the rest of the molecule is then washed away with more $CO_2$ (extraction).



Silver has been shown to possess very potent antimicrobial properties. Our method of loading silver nanoparticles promises to be a better way of making medical implants that resist infection and we are now exploiting this in collaboration with medical scientists at Nottingham.

The next page shows the way in which we are using $scCO_2$ to make biomedical materials.



For further reading on SCFs, see:-

- Jessop, P. G. & Leitner, W. (eds.) *Chemical Synthesis Using Supercritical Fluids* (Wiley-VCH, Weinheim, 1999).
- Poliakoff, M. & King, P. “Phenomenal fluids”, *Nature* **412**, 125 (2001).

**For information on any of the topics in this leaflet, contact**
**Prof. Martyn Poliakoff FRS, Prof. Steve Howdle or Dr. Mike George,**
**School of Chemistry, The University of Nottingham, Nottingham, NG7 2RD, UK**
**http://www.nottingham.ac.uk/supercritical/**

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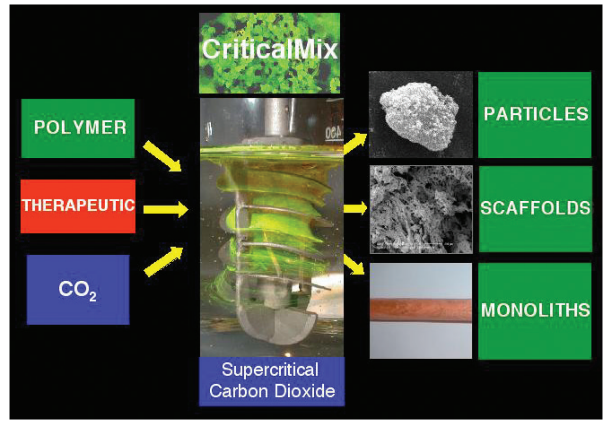
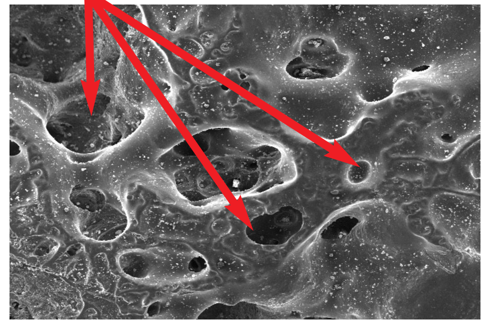
# *Biomaterials*

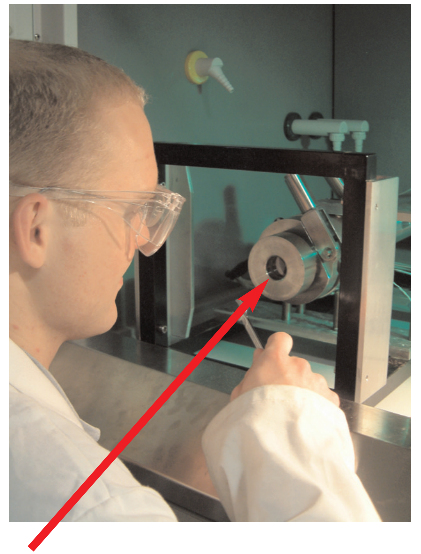
**SCFs provide new routes to polymeric biomaterials for medical applications. Cells from our body cannot form useful tissue by themselves. Polymer scaffolds are needed to act as a support to encourage cells to grow into new tissue. $scCO_2$ can be used to produce clean, porous scaffolds that contain active growth factors to encourage development of new tissue; so called tissue engineering.**



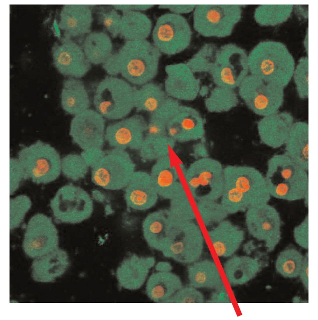
The gas-like properties of $CO_2$ ensure that it penetrates very effectively into polymers. In fact, under supercritical conditions, $CO_2$ dissolves in the polymer to such an extent that some polymers liquefy at close to room temperature. This process is called *plasticisation*. We have exploited it to mix other materials into the polymer such as pharmaceuticals, growth factors or enzymes. When the pressure is released, the $scCO_2$ escapes leaving behind a structure with controlled porosity that is suitable for tissue engineering.

There are many benefits of using $scCO_2$ to produce biomaterials. The process with $scCO_2$ is very clean; conventional solvents like $CHCl_3$ would leave behind toxic residues. The porosity can be controlled merely by changing the pressure of $scCO_2$ in the process or by varying the rate of releasing the $CO_2$. The most important feature is that that the pharmaceuticals or growth factors are unaffected by the $CO_2$. They retain all of their activity after processing; conventional methods cannot do this.





We have now shown that our scaffolds prepared using $scCO_2$ are very suitable for growing liver cells and bone cells. Successful cell growth on the scaffolds leads to new tissue being formed. The project has involved close collaboration between our group and tissue engineers at Nottingham and Southampton. Using the same technology we can also produce shaped materials for surgical use and polymer *microparticles* for controlled drug release systems. Again, the key to success is the plasticisation of the polymer and mixing followed by careful release of the $CO_2$. The work in biomaterials has also involved collaborations with industry as well as with scientists from the *Russian Academy of Sciences*



**For more information about Biomaterials using SCFs, read:-**

- Howdle, S. M.; Watson, M. S.; Whitaker, M. J.; Popov, V. K.; Davies, M. C.; Mandel, F. S.; Wang, J. D.; Shakesheff, K. M. “Supercritical Fluid Mixing: Preparation of Thermally Sensitive Polymer Composites Containing Bioactive Materials”, *Chem. Comm.*, 109-110 (2001).

- Yang, X. B.; Roach, H. I.; Clarke, N. M. P.; Howdle, S. M.; Quirk, R. A.; Shakesheff, K. M.; Oreffo, R. O. C. “Human osteoprogenitor growth and differentiation on synthetic biodegradable structures after surface modification”, *Bone*, **29**, 523 - 531 (2001).