Supercritical Fluid properties are of interest as being significantly different from liquids or gases in the area near the critical temperature, \( T_c \), and the critical pressure, \( P_c \). The primary physical feature of supercritical fluids in the immediate critical point region is the very pronounced change in density with pressure.

Critical region shown for carbon dioxide in terms of \( Pr \) and \( Tr \), the reduced properties. \( CO_2 \) is the most common supercritical solvent and the one for which we have the most information.
Supercritical Fluid Chromatography (SFC)

... an exact analog of gas chromatography or liquid chromatography. The supercritical fluid acts as a solvent. For industrial processes, capacity is the critical factor. The density of supercritical fluids is intermediate between that of gases and liquids. However the viscosity is lower so we can use higher velocity through the packing. Therefore it is expected that, while somewhat lower than liquids, the capacity of SFC can be sufficient to be of industrial interest.

Table 1. Transport Property Comparison

<table>
<thead>
<tr>
<th>Solvent Phase</th>
<th>Density (g cm(^{-3}))</th>
<th>Viscosity (centipoise)</th>
<th>Diffusivity (cm(^2) sec(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas</td>
<td>~0.001</td>
<td>0.005 - 0.035</td>
<td>0.01 - 1.0</td>
</tr>
<tr>
<td>SCF</td>
<td>0.2 - 0.9</td>
<td>0.02 - 0.1</td>
<td>0.1x10(^{-4}) - 3.3x10(^{-4})</td>
</tr>
<tr>
<td>Liquid</td>
<td>0.8 - 1.0</td>
<td>0.3 - 2.4</td>
<td>0.5x10(^{-5}) - 2.0x10(^{-5})</td>
</tr>
</tbody>
</table>

As an example of the dramatic effect of the property changes in the critical region the effect of pressure on the solubility of Naphthalene is shown to the left. The mole fraction of solubility, \(y_k\), varies by several orders of magnitude over a very short pressures range. Diffusivities and other transport properties behave in a similar manner. The first conclusion must be that if one is to maintain constant solvent properties, large pressure drops cannot be abided. On the other hand there are times when the pressure drop aids the separation. It is important to note that the effects upon diffusion are similar and the combined solubility and diffusion behavior provide some very interesting behavior when supercritical fluids are used in chromatography. Supercritical CO\(_2\) is a good solvent for nonpolar molecules like naphthalene, but performs less well with polar fluids.

SFC Advantages

Liquid chromatography is fairly readily adapted to industrial scale because sufficient feedstock can be passed through the chromatograph. On the other hand gas phase chromatography has a role primarily in the lab, because gas densities are 1000 times lower than the corresponding liquid phase. Supercritical Fluids lie in the middle ground, so there is hope to use some gas phase properties can be imparted to a high density solute. Typical transport properties at ambient temperatures for all three phases are given in the table immediately below.
Compared with HPLC, SFC provides rapid separations without the use of organic solvents. With the desire for environmentally conscious technology, the use of organic chemicals as used in HPLC could be reduced with the use of SFC.

In addition, SFC separations can be done faster than HPLC separations because the diffusion of solutes in supercritical fluids is about ten times greater than that in liquids (and about three times less than in gases). Decreased resistance to mass transfer in the column allows for fast high-resolution separations.

Compared with GC, capillary SFC can provide high-resolution chromatography at much lower temperatures. This allows fast analysis of thermolabile compounds.

A comparison of separation characteristics of the three types of chromatography is shown to the right. Here we show areas of applicability in a graph of number of places vs. separation factor for where $R_s = 1.5$ and $K=2$. SFC is much like liquid chromatography in capacity with improved separation. The open question concerns the price paid in the former in terms of increased dispersion. One can use all of the solvent tricks to modify the separation characteristics to one's advantage.

Mobile phase
There are a number of possible fluids that may be used in SFC as the mobile phase. However, based on its low cost, low interference with chromatographic detectors, and good physical properties (nontoxic, nonflammable, low critical values) carbon dioxide is the standard. The main disadvantage of carbon dioxide is its inability to elute very polar or ionic compounds.

Table 2. Typical Supercritical Solvents

<table>
<thead>
<tr>
<th>Compound</th>
<th>$T_e$ °C</th>
<th>$P_e$ atm</th>
<th>$d^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂</td>
<td>31.3</td>
<td>72.9</td>
<td>0.96</td>
</tr>
<tr>
<td>C₃H₄</td>
<td>9.9</td>
<td>50.5</td>
<td>---</td>
</tr>
<tr>
<td>N₂O</td>
<td>36.5</td>
<td>72.5</td>
<td>0.94</td>
</tr>
<tr>
<td>NH₃</td>
<td>132.5</td>
<td>112.5</td>
<td>0.40</td>
</tr>
<tr>
<td>n-C₅</td>
<td>196.6</td>
<td>33.3</td>
<td>0.51</td>
</tr>
<tr>
<td>n-C₄</td>
<td>152.0</td>
<td>37.5</td>
<td>0.50</td>
</tr>
<tr>
<td>CCl₂F₂</td>
<td>111.8</td>
<td>40.7</td>
<td>1.12</td>
</tr>
<tr>
<td>CHF₃</td>
<td>25.9</td>
<td>46.9</td>
<td>----</td>
</tr>
<tr>
<td>H₂O</td>
<td>374.1</td>
<td>218.3</td>
<td>----</td>
</tr>
</tbody>
</table>
Pure supercritical carbon dioxide is a relatively non-polar solvent, but has some limited affinity with polar molecules due to its large molecular quadrupole. Modifiers can often be added to improve the solubility of polar molecules (ex. MEOH, EtOH, water, amines). Both ISOCRATIC and GRADIENTS can be run in SFC.

The addition of the modifier fluid improves the solvating ability of the supercritical fluid and sometimes enhances selectivity of the separation. It can also help improve separation efficiency by blocking some of the highly active sites on the stationary phase.

Modifier fluids are commonly used, especially in packed column SFC. **Co-solvents** Generally the cosolvent or modifier is a material added to the supercritical solvent at low percentage, which makes a significant change to the solvent properties. For example the selectivity ($\alpha$) of 2-naphthol with respect to anthracene can be enhanced greatly by adding methanol to supercritical CO$_2$. Unmodified CO$_2$ will give a selectivity of about 7. It rises to 30 it 3.5% methanol is added as a cosolvent. Predicting cosolvent effects is difficult-dealing with exchange between surfaces and mixed solvent.

- work has focused on proton acceptors or donors.
- dipolar molecules, surfactants and other more complex molecules.
- hydrogen bonding is an area where significant work is still required.

The concept of producing gradients in co-solvents promises to be a powerful weapon.

The figure to the left shows the result on solubility of modifying co-solvents in the in a chromatographic separation or ortho benzoic acid. Note that both cosolvents have a dramatic effect upon solubility - almost a factor of a 50 at the lower pressures. As the pressure rises, the methanol proves to be the better cosolvent. It is an interesting exercise to theorize why this trend occurs.
A typical SFC analytical chromatograph. It is only different from standard analytical chromatographs in that equipment is needed to program and control the supercritical fluid.

**Columns (stationary phase)**
- Typically stainless steel packed columns
- Small bores are common (250 and 530 µm) packed with 5 µm particles
- Same types of stationary phase materials as either normal or reverse phase HPLC

Open bore (capillary columns can also be used)

**Detectors**

Modified versions of GC or HPLC detectors

Must accommodate high pressures (mostly for HPLC type detectors) and large solvent volumes produced during decompression (mostly for GC type detectors).
First we will compare the separation polyaromatic heterocycles (PAH) by methods specific to the three different methods. The coal tar separation shown here using three methods indicates the type of differences one encounters using the three methods. If we select gas chromatography, with a temperature gradient from 80°C to 250°C over the 50-minute retention time, we end up with a reasonable separation. Cooling the column would have to be added to the time of separation.

Using a Polarity gradient in HPLC going from 50 to 100% acrylonitrile, an acceptable separation can be effected in forty minutes.

Turning finally to SFC, a pressure ramp is used in the solvent, such that solvent density rose from 0.225g/L to 0.7 g/ml over the retention period of 120 minutes. Certainly the last is not the best analytical solution, however, it does eliminate the need for acrylonitrile recover and recycle. The recompression of the supercritical solvent would seem to be simpler.
SFC Separation of Polymer Samples

DC silicone fluid separation
SE-54 10m x 50um ID x 0.25um Df
Carbon dioxide 100 C, 100 bar