

diameters. Such a diameter would cater for production rates of both speciality and commodity materials. At the time of composing this chapter, the largest diameter COBR installed in industrial operation is 60 mm ID at a flow rate of  $0.115 \text{ m}^3 \text{ min}^{-1}$ .

### 3.3.5.2 Scale Down

Due to the limited availability of new drug compounds, scaling down COBC becomes necessary, albeit challenging. Some work on meso COBR and meso structures<sup>77</sup> has been reported considering fluid mechanics<sup>51,77–83</sup> and applications<sup>84–91</sup> together with some confidential work on COBCs of 10, 8, 4 and 2 mm ID by NiTech funded by DTI and the Scottish Enterprise.<sup>92</sup> In addition, studies on mixing performance<sup>93–96</sup> and applications<sup>97–99</sup> using hollow micro-capillary tubes were also carried out.

For micro devices it is generally regarded that the diameter/width of the flow channel is smaller than 1 mm; however, the cut-off between meso and macro devices is less clear. In this book chapter, I categorize meso devices as having diameters of tube from 1 to 10 mm and macro COBC having diameters above 10 mm, for the purpose of simplification.

At a scale, the motion of fluids is governed by the Navier–Stokes equation, which is  $f = ma$ , written for a viscous fluid. It satisfies the conservation of mass, momentum and energy, where mass conservation is included implicitly through the continuity equation. The combined form for incompressible fluids is given as

$$\frac{\partial u}{\partial t} + u \cdot \nabla u = -\frac{1}{\rho} \nabla p + \frac{\mu}{\rho} \nabla^2 u + \frac{F}{\rho} \quad (3.1)$$

where  $p$  is the pressure ( $\text{kN m}^{-2}$ ),  $\mu$  the viscosity ( $\text{Ns m}^{-2}$ ),  $F$  the body force (N) and  $u$  the flow velocity ( $\text{m s}^{-1}$ ). The terms on the left of eqn (3.1) are the inert force and the terms on the right denote the pressure, viscous and external forces applied to the fluid. Does the flow velocity,  $u$ , have a range outside which the eqn (3.1) is invalid?

At macroscopic level, most forms of mixing, *e.g.* oscillating, stirring, turbulent flow, are convective motions, effectively to break and reduce the length scale, allowing diffusion to take place and increasing the local magnitude of mass transfer by diffusion. The upper limit for the flow velocity in the Navier–Stokes equation is equal or lower than the speed of sound.<sup>100</sup>

In small-scale flows, however, the Navier–Stokes description is expected to fail<sup>101,102</sup> when the characteristic hydrodynamic lengthscale approaches the fluid “internal” lengthscale.<sup>103</sup> What is then the fluid “internal” lengthscale? Taking a water molecule for example, it has a size scale of  $10^{-10}$  m. In order to satisfy the continuum equations, we need to define the macroscopic variables, *e.g.* how many molecules are needed to draw a reliable average? 10 is probably too few; 100 seems to be reasonable ( $10^{-8}$  m). This means that each “point” in a water continuum is a box with the side about 0.01  $\mu\text{m}$ . To satisfy