More important in bacterial and fungal fermentations is *wall growth*. If cells adhere to surfaces, and if such adherent cells have altered metabolism (e.g., due to mass transfer limitations), then data obtained in a small fermenter may be unreliable in predicting culture response in a larger fermenter. This point is more clearly illustrated in Example 10.2.

Perhaps even more importantly, it can be shown that the physical conditions in a large fermenter can never exactly duplicate those in a smaller fermenter if *geometric similarity* is maintained. In the case described in Table 10.2, a stirred-tank diameter has been increased by a factor of 5, resulting in a 125-fold increase in volume, since the height-to-diameter ratio was maintained constant. Four cases are treated in Table 10.2: scale-up based on constant power input (P_0/V), constant liquid circulation rate inside the vessel (pumping rate of impeller per unit volume, Q/V), constant shear at impeller tip (ND_i), and constant Reynolds number ($ND_i^2\rho/\mu$). Note that $P \propto N^3D_i^5$, $V \propto D_i^3$, $Q \propto ND_i^3$, $P/V \propto N^3D_i^2$, and $Q/V \propto N$. Thus, fixing N and D_i fixes all the quantities in Table 10.2. Since these quantities have different dependencies on N and D_i, a change of scale *must result* in changes in the physical environment that the cells experience. When these changes alter the distribution of chemical species in the reactor, or they destroy or injure cells, the metabolic response of the culture will differ from one scale to another. In some cases cells respond to modest changes in mechanical stress by changing physiological functions even when there is no visible cell injury or cell lysis. Thus, different scale-up rules (constant P/V implies constant OTR, constant Re implies geometrically similar flow patterns, constant N to give constant mixing times, and constant tip speed to give constant shear) can give very different results.

These scale-up problems are all related to transport processes. In particular, the relative time scales for mixing and reaction are important in determining the degree of heterogeneity in a fermenter. As we scale up, we may move from a system where the microkinetics (the cellular reactions) control the system response at small scale to one where transport limitations control the system response at large scale. When a change in the controlling regime takes place, the results of small-scale experiments become unreliable with respect to predicting large-scale performance.

TABLE 10.2 Interdependence of Scale-up Parameters

			Production fermenter, 10,000:l			
Scale-up criterion	Designation	Small fermenter, 80 l	Constant, P_0/V	Constant, N	Constant, $N \cdot D_i$	Constant, Re
Energy input	P_0	1.0	125	3125	25	0.2
Energy input/volume	P_0/V	1.0	1.0	25	0.2	0.0016
Impeller rotation number	N	1.0	0.34	1.0	0.2	0.04
Impeller diameter	D_i	1.0	5.0	5.0	5.0	5.0
Pump rate of impeller	Q	1.0	42.5	125	25	5.0
Pump rate of impeller/volume	Q/V	1.0	0.34	1.0	0.2	0.04
Maximum impeller speed (max. shearing rate)	$N \cdot D_i$	1.0	1.7	5.0	1.0	0.2
Reynolds number	$ND_i^2\rho/\mu$	1.0	8.5	25.0	5.0	1.0

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