

Consequently, Eq. (9.34) can be subdivided as follows:

$$\bar{v}_{\text{total}} = \ln \frac{N_0}{N} = \bar{v}_{\text{heating}} + \bar{v}_{\text{holding}} + \bar{v}_{\text{cooling}} \quad (9.35)$$

$$\bar{v}_{\text{heating}} = \ln \frac{N_0}{N_1} = \int_0^{t_1} k dt = \alpha' \int_0^{t_1} e^{-E/RT} dt \quad (9.36)$$

$$\begin{aligned} \bar{v}_{\text{holding}} &= \ln \frac{N_1}{N_2} = \int_0^{t_2} k dt = \alpha' \int_0^{t_2} e^{-E/RT} dt \\ &= \alpha' e^{-E/RT} t_2 \end{aligned} \quad (9.37)$$

$$\bar{v}_{\text{cooling}} = \ln \frac{N_2}{N} = \int_0^{t_3} k dt = \alpha' \int_0^{t_3} e^{-E/RT} dt \quad (9.38)$$

$$t = t_1 + t_2 + t_3 \quad (9.39)$$

where

$N$  = sterility level (number of contaminating microbes after sterilization)

$N_0$  = contamination level (number of contaminating microbes before sterilization)

$N_1$  = number of contaminating microbes after heating period,  $t_1$

$N_2$  = number of contaminating microbes after holding period,  $t_2$

Supposing that the temperature-time profile is given as shown in Table 9.2, it is possible to calculate each term of  $\bar{v}$  for heating and cooling, but the analytical solution seems to be tedious. Accordingly, the graphical rather than the analytical solution to this subject will be discussed.

### 9.3.2. Example of calculation

A medium in a fermentor is sterilized batchwise at 120°C. The temperature-time profile observed with a recorder attached to the fermentor is as follows:

$t$ (min)	0 10 30 36 43 50 55 58 63 70 102 120 140
$T'$ (°C)	30 50 90 100 110 120 120 110 100 90 60 44 30

Assuming that the specific denaturation rate of contaminating bacterial spores,

$$k = 7.94 \times 10^{38} \exp\left(-\frac{68.7 \times 10^3}{RT}\right) \text{ min}^{-1} \quad (\text{cf. Fig. 9.3})$$

and that the initial number of the spores,  $N_0 = 6 \times 10^{12}$ , calculate the sterility level after the sterilization.

**Solution**

Figure 9.11 shows the temperature-time profile and the values of  $k$  as a function of  $t$ . A graphical integration yields:

$$\int_{t=34}^{t=64} k dt = 33.8$$

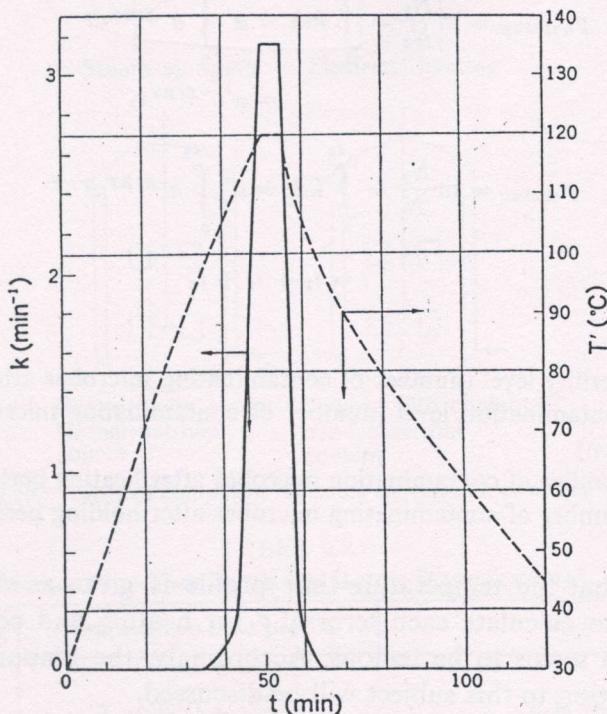


Fig. 9.11.  $k \text{ min}^{-1}$  and  $T' \text{ }^{\circ}\text{C}$  vs.  $t \text{ min}$ ; example of calculation.

Regarding the periods before  $t=34$  min and after  $t=64$  min, the values of  $k$  are small enough to be neglected.

$$\begin{aligned} 1 - P &= N_0 e^{-kt} \\ &= 6 \times 10^{12} \times e^{-33.8} \\ &= 1.5 \times 10^{-2} \quad (\text{cf. Fig. 9.9}) \end{aligned}$$

## 9.4. CONTINUOUS STERILIZATION OF MEDIA

### 9.4.1. Equipment and temperature-time profile

Figure 9.12 shows equipment for continuous sterilization of fermentation media.

The upper projected instant medium holding an exp

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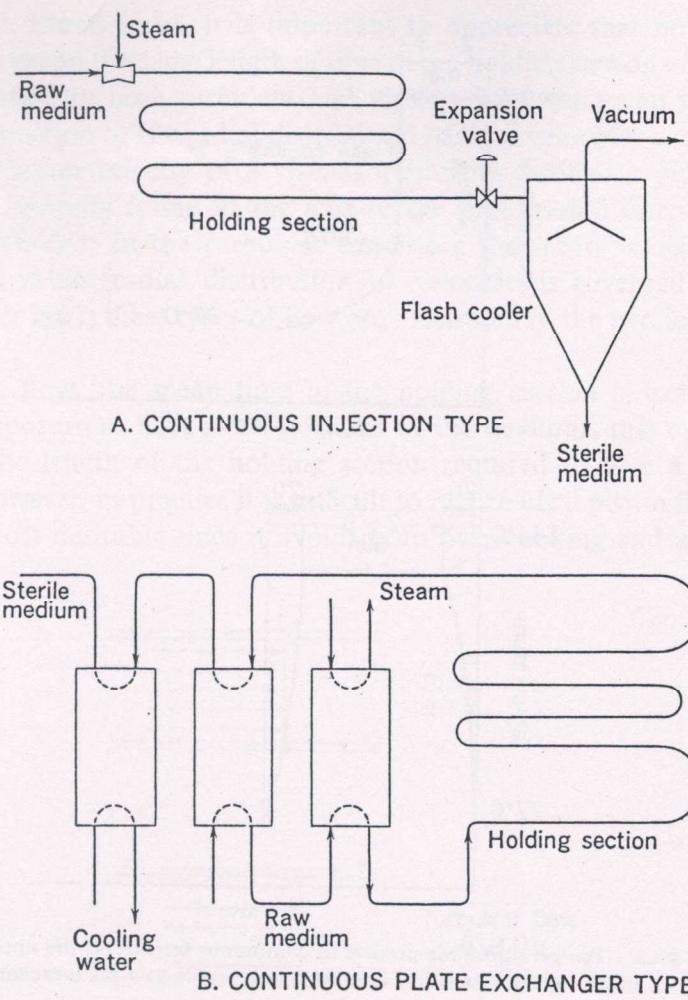


Fig. 9.12. Continuous sterilizers.

The upper part, A, of the figure shows an injection-type sterilizer; steam is injected directly into the raw medium; therefore the temperature rises almost instantly to the predetermined sterilizing temperature. The time for which the medium is held at this temperature is governed by the length of a pipe in the holding section. The sterilized medium is cooled instantly by passing through an expansion valve into a vacuum chamber, as shown in the figure.

An example of the temperature-time profile obtained with injection-type equipment is shown in the upper profile of Fig. 9.13. The numerical values given in the figure have no general significance; they will depend on the particular sterilization problem. Because of the short period of exposure to heat, it is possible to raise the temperature as high as 140°C without serious damage to the medium.

The lower part, B, of Fig. 9.12 shows a plate heat exchanger of the type fre-

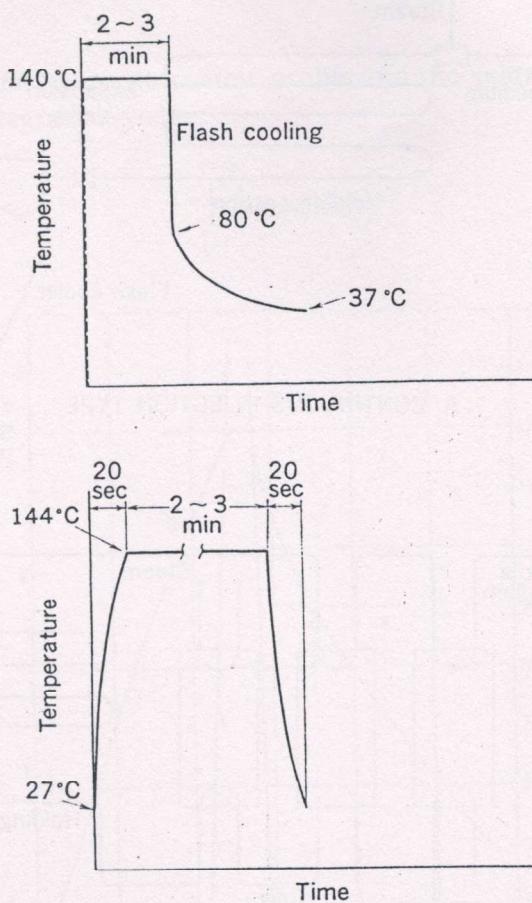


Fig. 9.13. Temperature-time profiles in continuous sterilizers; the upper profile applies to a steam injection sterilizer and the lower profile to a plate-exchanger sterilizer.

quently employed in the fermentation industry for the continuous sterilization of media.

Steam-heated plates raise the temperature of the raw medium, the medium is maintained at the elevated temperature for a certain period of time, and then cooled in another section of the plate exchanger, as shown in Fig. 9.12.

Although the time required to heat and cool the raw medium is much longer than with the steam injection type of continuous sterilization, the contribution of these periods to the sterilizing cycle will be much smaller (around 1 or 2%) than in the case with batch sterilization (*cf.* the lower profile in Figs. 9.13 and 9.11).

#### 9.4.2. Residence time concept

To design and evaluate a continuous media sterilizer where the raw medium

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passes through round pipes, it is important to appreciate that not all portions of the medium spend the same length of time in the holding section of the sterilizer.

This is because, in both turbulent and viscous flow, the mean velocity,  $\bar{u}$ , of the fluid is a function of the radial distribution of fluid velocities occurring across the pipe. The mean velocity of a viscous-fluid flow through a pipe is one-half the maximum velocity found at the axis of the pipe (radial distribution of velocities is parabolic); in the turbulent condition, the mean velocity is 82% of the maximum value (radial distribution of velocities is governed by Karman-Prandtl's power law); these types of flow are illustrated in the two lower diagrams of Fig. 9.14.

With piston flow, the mean time in the holding section is exactly equal to the time of exposure to heat in all portions of the medium; this makes it easier to calculate the length of the holding section required to give a desired level of sterility. However, in practice it is difficult to realize ideal piston flow, although it would be most desirable since it avoids both over-cooking and under-cooking the medium.

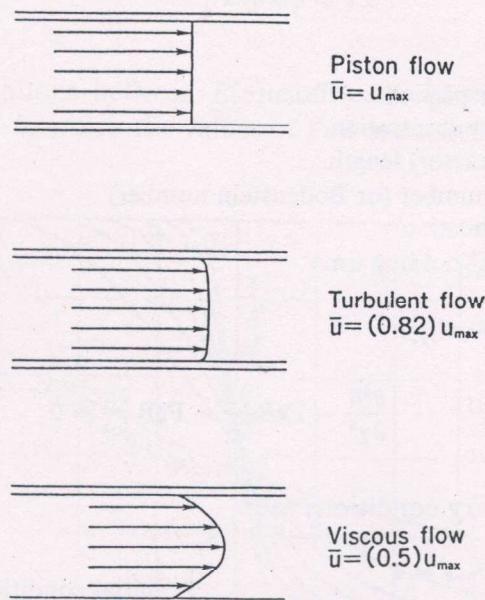


Fig. 9.14. Distribution of velocities in fluids exhibiting different types of flow inside round pipes;  $\bar{u}$  = mean velocity of the fluid.

It is difficult to predict the distribution of residence times in advance, so this must be determined empirically. This can be done by discharging a "marker" material and observing the pattern of its recovery at the outlet of the pipe; this pattern will, of course, be dependent on the type of flow in the pipe.

Before proceeding to the following discussion, it is important to make an underlying assumption clear. The assumption is that, as the length of pipe in

the holding section becomes longer, the property of effective dispersion is more satisfactory than the distribution of velocities to describe the performance of sterilizers. This is particularly true for sterilizers where elbows or valves are present, to say nothing of the more complicated pathways existing in the plate-type heat exchanger.

The behavior of microbes suspended in a medium is considered to follow closely the mixing characteristics of the equipment with respect to effective dispersion, originating from the mixing of molecules.<sup>2</sup>

For simplicity, the residence time curves for a pipe will be considered. A differential equation is derived from the material balance as follows:

$$E_z \frac{\partial^2 \bar{n}}{\partial x^2} - \bar{u} \frac{\partial \bar{n}}{\partial x} = \frac{\partial \bar{n}}{\partial t} \quad (9.40)$$

Setting

$$\bar{n} = n/n_0, \quad \chi = x/L, \quad \text{PeB} = \bar{u}L/E_z, \quad \phi = t/\bar{t}$$

where

$E_z$  = axial dispersion coefficient

$n_0$  = initial concentration

$L$  = pipe (reactor) length

$\text{PeB}$  = Péclet number (or Bodenstein number)

$x$  = axial direction

$\bar{t}$  = nominal holding time

The exit concentra-

$$\bar{n}_{\chi=1} = R(\phi)$$

$$= 16 \sum_{r=1}^{\infty} \frac{1}{r^2} \frac{1}{1 + \frac{4\lambda_r^2}{\text{PeB}} \phi} \quad (1)$$

where

Numerical correlat  
shown in Fig. 9.15,<sup>7</sup> in

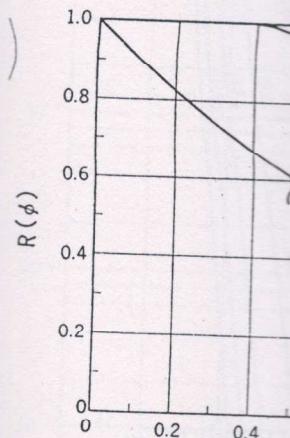


Fig. 9.15. Effect of differ  
of the holding time,  $t$ , to

Rearranging Eq. (9.40),

$$\frac{\partial^2 \bar{n}}{\partial \chi^2} - \text{PeB} \frac{\partial \bar{n}}{\partial \chi} - \text{PeB} \frac{\partial \bar{n}}{\partial \phi} = 0 \quad (9.41)$$

Initial and boundary conditions are:

$$\left. \begin{array}{l} \chi > 0, \quad \bar{n}_{\phi=0} = 1 \\ \chi < 0, \quad \bar{n}_{\phi=0} = 0 \\ \chi \rightarrow 0^+, \quad \frac{\partial \bar{n}}{\partial \chi} - \text{PeB} \bar{n} = 0 \\ \chi \rightarrow 1, \quad \frac{\partial \bar{n}}{\partial \chi} = 0 \end{array} \right\} \begin{array}{l} \text{initial conditions} \\ \text{boundary conditions} \end{array}$$

Solving for  $\bar{n}$ <sup>7,18</sup>

$$\bar{n} = 32 \sum_{r=1}^{\infty} \frac{\text{PeB} \lambda_r (4\lambda_r^2 \cos 2\lambda_r \chi + \text{PeB} \sin 2\lambda_r \chi)}{(16\lambda_r^2 + 4\text{PeB} + \text{PeB}^2)(16\lambda_r^2 + \text{PeB}^2)} \exp \left( \frac{\text{PeB}}{2} \chi - \frac{\text{PeB}^2 + 16\lambda_r^2}{4\text{PeB}} \phi \right) \quad (9.42)$$

It is seen from the fig  
flow as the values of Pe  
heated at all in the cas  
any type of flow can be

provided: the  $\lambda_r$  ( $r=1, 2, 3, \dots$ ) are the positive roots, taken in order of magnitude, of the transcendental equation

$$\tan 2\lambda = \frac{8\lambda PeB}{16\lambda^2 - PeB^2} \quad (9.43)$$

The exit concentration,  $\bar{n}_{\chi=1}$ , is given from Eq. (9.42) by setting  $\chi=1$ .

$$\begin{aligned} \bar{n}_{\chi=1} &= R(\phi) \\ &= 16 \sum_{r=1}^{\infty} \frac{\lambda_r \sin 2\lambda_r}{(16\lambda_r^2 + 4PeB + PeB^2)} \exp \left( \frac{PeB}{2} - \frac{PeB^2 + 16\lambda_r^2}{4PeB} \phi \right) \end{aligned} \quad (9.44)$$

where

$$E(\phi) = - \frac{dR(\phi)}{d\phi}$$

$$\int_0^{\infty} E(\phi) d\phi = 1.0$$

Numerical correlations between  $R(\phi)$  and  $\phi$  are plotted from Eq. (9.44) as shown in Fig. 9.15,<sup>7</sup> in which the values of PeB are taken as parameters.

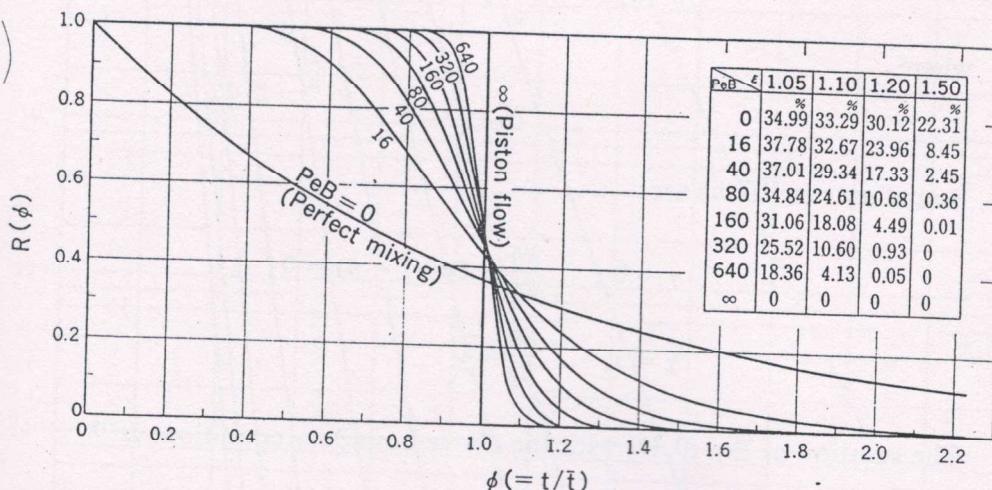


Fig. 9.15. Effect of different types of flow (as shown by different PeB values and different ratios of the holding time,  $t$ , to the nominal holding time,  $\bar{t}$ ), in continuous sterilization of media.

It is seen from the figure that the flow in the reactor approaches piston-type flow as the values of PeB are increased. Assuming that the medium is not overheated at all in the case of piston flow, the relative degree of overheating for any type of flow can be defined as

$$\int_{\xi}^{\infty} E(\phi) d\phi = R(\xi) \quad (9.45)$$

provided:

$\xi$  = dimensionless residence time ( $\xi > \phi = 1$ )  
 $E(\phi)$  = residence time distribution function

Some values of  $R(\xi)$  are listed in Fig. 9.15.<sup>7</sup>

Next, the inactivation of organisms by heat in continuous sterilizers will be considered. Since the rate of microbial death is expressed by Eq. (9.1), the material balance with a continuous sterilizer (straight pipe) at steady state is as follows:

$$Ez \frac{d^2n}{dx^2} - \bar{u} \frac{dn}{dx} - kn = 0 \quad (9.46)$$

Changing the variables as shown previously in connection with Eq. (9.40) and rearranging Eq. (9.46),

$$\frac{d^2\bar{n}}{d\chi^2} - PeB \frac{d\bar{n}}{d\chi} - PeBN_r \bar{n} = 0 \quad (9.47)$$

where

$$N_r = kL/\bar{u}$$

Boundary conditions are:

$$\chi \rightarrow 0^+, \quad \frac{d\bar{n}}{d\chi} + PeB(1 - \bar{n}) = 0$$

$$\chi = 1, \quad \frac{d\bar{n}}{d\chi} = 0$$

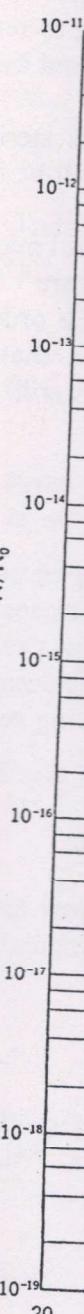
The solution of Eq. (9.47) with the above boundary conditions is:<sup>19</sup>

$$\begin{aligned} \bar{n}_{\chi=1} &= (n/n_0)_{\chi=L} \\ &= \frac{4\zeta e^{PeB/2}}{(1 + \zeta)^2 e^{PeB/2} - (1 - \zeta)^2 e^{PeB/2}} \end{aligned} \quad (9.48)$$

provided:

$$\zeta = \sqrt{1 + \frac{4N_r}{PeB}}$$

Fig. 9.16. 1



A degree of sterility,  $N/N_0$ , is plotted against,  $N_r (= kL/\bar{u})$  in Fig. 9.16 according to Eq. (9.48), parameters being PeB ( $= \bar{u}L/E_z$ ).

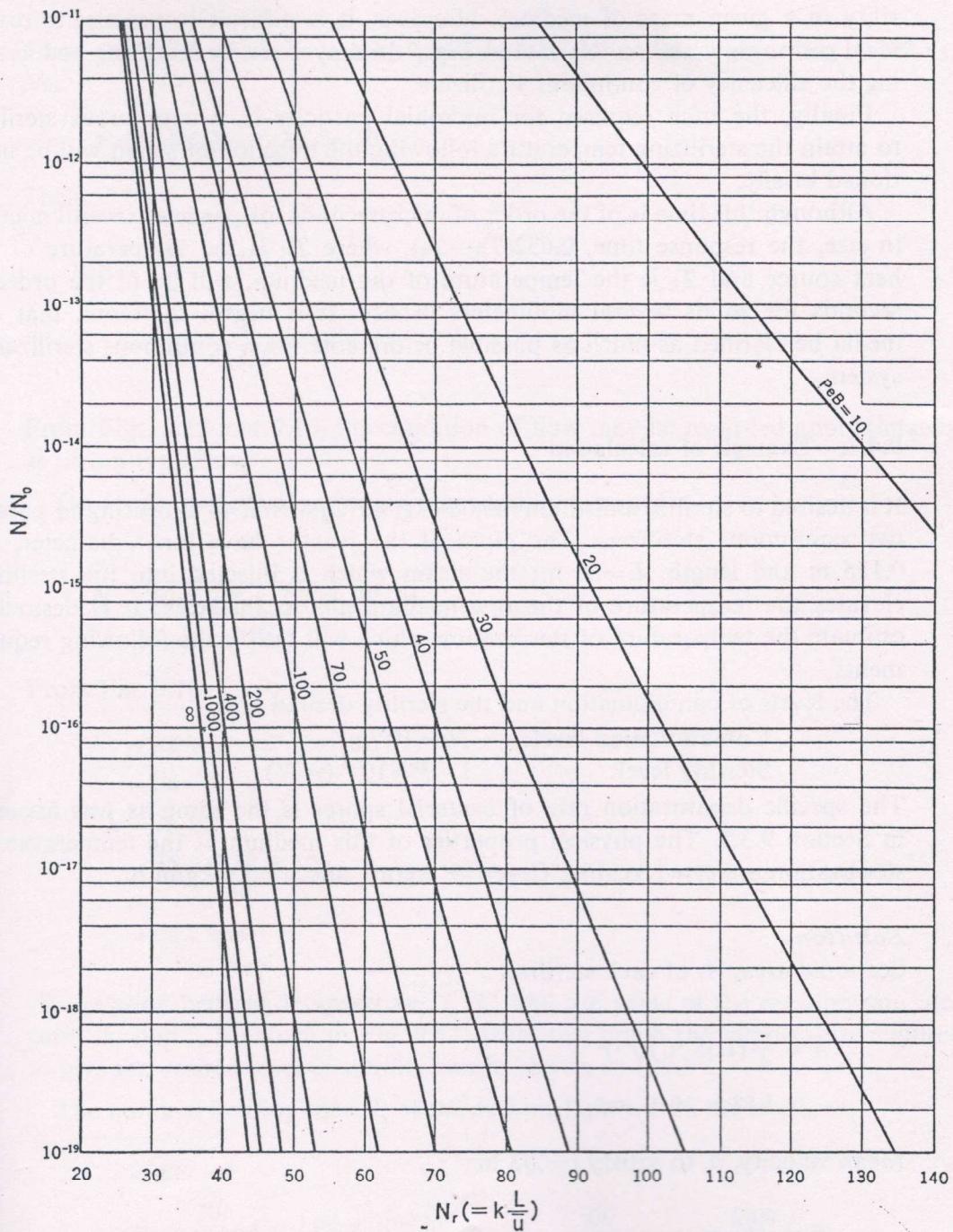


Fig. 9.16. Effect of different types of flow (as shown by different PeB values) on the destruction of organisms ( $N/N_0$ ) at different rates of destruction (measured as  $N_r = kL/\bar{u}$ ).

It is also evident from Fig. 9.16 that where  $PeB = \infty$ , in other words with ideal piston flow, conditions are most favorable for designing continuous sterilizers, since this reduces the length of pipe required to produce a given degree of sterility in a given mass of medium. However, it is difficult in practice to realize ideal piston flow and so the data in Fig. 9.16 may assist in designing and assessing the efficiency of continuous sterilizers.

Finally, the time required for microbial particles in a continuous sterilizer to attain the sterilizing temperature following the injection of steam will be mentioned briefly.

Although this time is of the order of microseconds for particles several microns in size, the response time,  $0.632(T_H - T_0)$ , where  $T_H$  is the temperature of the heat source and  $T_0$  is the temperature of the medium, will be of the order of seconds for solids several millimeters in size. It is urged, therefore, that raw media be clarified as much as possible before entering a continuous sterilization system.

#### 9.4.3. Example of calculation

It is desired to sterilize a medium (60,000 kg, 40°C) within 40 min using in parallel two continuous sterilizers. The pipes of the reactor have inner diameter,  $d = 0.155$  m and length,  $L = 50$  m; the steam which is injected into the sterilizers elevates the temperature of the raw medium almost instantly. It is desired to estimate the temperature of sterilization which will satisfy the following requirements.

The levels of contamination and the sterility desired are:

Contamination level:  $N_0 = 10^5/\text{ml}$

Sterility level:  $1 - P = 10^{-3} (= N)$

The specific denaturation rate of bacterial spores is the same as was assumed in Section 9.3.2. The physical properties of this medium at the temperature of sterilization are  $c_p = 1 \text{ kcal/kg°C}$ ,  $\rho = 10^3 \text{ kg/m}^3$ , and  $\mu = 3.6 \text{ kg/m hr}$ .

#### Solution

Sectional area,  $A$ , of each sterilizer:

$$A = \frac{\pi}{4} (1.55 \times 10^{-1})^2$$

$$= 1.88 \times 10^{-2} \text{ m}^2$$

Mean velocity,  $\bar{u}$ , to satisfy  $t = 2/3 \text{ hr}$ :

$$\bar{u} = \frac{60/2}{At} = \frac{30}{(1.88 \times 10^{-2})(2/3)}$$

$$= 2.39 \times 10^3 \text{ m/hr}$$