APPENDIX 2

The ratio between the rate of DNA synthesis in a culture after inhibition of DNA synthesis for one mass doubling to the rate of DNA synthesis in the same culture before the start of this inhibition (RSF).

Since the rate of DNA synthesis in a culture is the product of the number of forks in the culture multiplied by the velocity with which any one fork travels along the chromosome (F x V; Maaløe, 1961) RSF can be calculated if: (a) the same assumptions accepted in Appendix 1 are made, (b) the velocity of replication before and after the treatment is known (V_0 and V_1 respectively), and (c) the number of forks added to the culture in the course of this treatment (ΔF) is known, as a function of the number of forks present in the culture before the start of this treatment (F_0). By definition:

$$RSF = \frac{V_1 \cdot (F_0 + \Delta F)}{V_0 \cdot F_0} \tag{13}$$

If, for the sake of simplicity $V_0 = V_1$ (assumption (f) in the Introduction), then the problem remains to find the correlation between ΔF and F_0.

It was shown in Appendix 1 that

$$F_0 = 2^{C/\tau} - 1 \tag{5}$$

in a culture in a steady state of exponential growth. ΔF can be calculated, again with reference to Fig. 23, if the same assumptions as those made in Appendix 1 are accepted:

(a)

$$\Delta F = \frac{2\cdot\int_{0}^{1} f(x)dx}{\int_{0}^{C/\tau} f(x)dx + 2\cdot\int_{C/\tau}^{1} f(x)dx} = \frac{2}{2 - 2^{1-C/\tau} + 2.2^{1-C/\tau} - 2} =$$

$$\frac{2}{2^{1-C/\tau}} = 2^{C/\tau},$$

(b)

$$\Delta F = \frac{2\cdot\int_{0}^{2-(C+D)/\tau} f(x)dx + 4\cdot\int_{2-(C+D)/\tau}^{1} f(x)dx}{\int_{0}^{1-D/\tau} f(x)dx + 2\cdot\int_{1-D/\tau}^{1} f(x)dx} =$$

$$\frac{2 - 2.2^{(C+D)/\tau-1} + 4.2^{(C+D)/\tau-1} - 4}{2 - 2^{D/\tau} + 2.2^{D/\tau} - 2} = 2^{C/\tau},$$

(c) This case is equivalent to (b) for the purpose of this calculation (see Fig. 23),

(d)

$$\Delta F = \frac{4\cdot\int_{0}^{3-(C+D)/\tau} f(x)dx + 8\cdot\int_{3-(C+D)/\tau}^{1} f(x)dx}{\int_{0}^{1-D/\tau} f(x)dx + 2\cdot\int_{1-D/\tau}^{1} f(x)dx} =$$

$$\frac{4.2 - 4.2^{(C+D)/\tau-2} + 8.2^{(C+D)/ -2} - 8}{2 - 2^{D/\tau} + 2.2^{D/\tau} - 2} = 2^{C/\tau},$$

and for the general form

$$(n)\ \Delta F = \frac{2^n \cdot \int_0^{(n+1)-(C+D)/\tau} f(x)dx + 2^{n+1} \cdot \int_{n+1-(C+D)/\tau}^{1} f(x)dx}{\int_0^{1-D/\tau} f(x)dx + 2 \cdot \int_{1-D/\tau}^{1} f(x)dx} =$$

$$\frac{2^n.2 - 2^n.2^{(C+D)/\tau-n} + 2^{n+1}.2^{(C+D)/\tau-n} - 2^{n+1}}{2 - 2^{D/\tau} + 2.2^{D/\tau} - 2} =$$

$$\frac{2^{(C+D)/\tau}}{2^{D/\tau}} = 2^{C/\tau}.$$

Thus, for all values of τ and C

$$\Delta F = 2^{C/\tau} \tag{14}$$

$$\text{Since } F_o = 2^{C/\tau} - 1 \tag{5}$$

$$\text{then, } F_o + \Delta F = 2^{C/\tau+1} - 1 \tag{15}$$

$$\text{and} \quad RSF = \frac{2^{C/\tau+1} - 1}{2^{C/\tau} - 1} \tag{10}$$

The variation of RSF with C and with τ is shown in Fig. 2. This function has a lower limit (mathematically) as well as an upper limit (biologically):

(a) Mathematically, $\lim_{C/\tau \to \infty} RSF = 2$ (16).

In practice, however, in normal <u>thy</u>$^+$ bacteria the minimal value obtained for τ is 20 minutes where C = 40 minutes. Hence the minimal value for RSF is 2.33.

In this study the highest C obtained was 120 minutes, and $\tau \cong$ 40 minutes, making $C/\tau \cong 3$, and a lower limit of 2.14 for RSF.

(b) On the other hand, it was shown (Helmstetter <u>et al</u>, 1968) that C cannot be shorter than $2\tau/3$ in <u>E.coli</u> B/r. Therefore, at least in this strain the upper limit for RSF is

$$\mathrm{RSF}_{\max} = \frac{2^{2\tau/3\tau+1} - 1}{2^{2\tau/3\tau} - 1} = \frac{2^{5/3} - 1}{2^{2/3} - 1} \cong 3.7 \ .$$

APPENDIX 3

Average Number of Forks per Cell (FPC) in Steady State Exponentially Growing Cultures of Bacteria

This can be derived, again, using the same assumptions made in Appendices 1 and 2 (Introduction, assumptions (b), (e) and (g)), and with reference to Fig. 23:

(a)

$$\mathrm{FPC} = \int_{0}^{1-D/\tau} f(x)dx = 2 - 2^{D/\tau} = 2^{D/\tau}\,(2^{1-D/\tau} - 1) = 2^{D/\tau}\,(2^{C/\tau} - 1),$$

(b)

$$\mathrm{FPC} = \int_{0}^{1-D/\tau} f(x)dx + 2 \cdot \int_{2-(C+D)/\tau}^{1} f(x)dx = 2 - 2^{D/\tau} + 2.2^{(C+D)/ -1} -$$

$$- 2 = 2^{D/\tau}\,(2^{C/\tau} - 1),$$

(c)

$$\mathrm{FPC} = \int_{0}^{2-(C+D)/\tau} f(x)dx + 3 \cdot \int_{2-(C+D)/\tau}^{1-D/\tau} f(x)dx + 2 \cdot \int_{1-D/\tau}^{1} f(x)dx =$$

$$2 - 2^{(C+D)/\tau-1} + 3.2^{(C+D)/\tau-1} - 3.2^{D/\tau} + 2.2^{D/\tau} - 2 = 2^{D/\tau}(2^{C/\tau} - 1)$$

(d)

$$\mathrm{FPC} = 3. \int_{0}^{3-(C+D)/\tau} f(x)dx + 7 \cdot \int_{3-(C+D)/\tau}^{1-D/\tau} f(x)dx + 6 \cdot \int_{1-D/\tau}^{1} f(x)dx =$$

$$3.2 - 3.2^{(C+D)/\tau-2} + 7.2^{(C+D)/\tau-2} - 7.2^{D/\tau} + 6.2^{D/\tau} - 2 = 2^{D/\tau}(2^{C/\tau} - 1),$$

and for the general case

(n)

$$FPC = (2^n - 1) \cdot \int_0^{n+1-(C+D)/\tau} f(x)dx + (2^{n+1} - 1) \cdot \int_{n+1-(C+D)/\tau}^{1-D/\tau} f(x)dx +$$

$$+ (2^{n+1} - 2) \cdot \int_{1-D/\tau}^{1} f(x)dx =$$

$$2^n \cdot 2 - 2^n \cdot 2^{(C+D)/\tau-n} - 2 + 2^{(C+D)/\tau-n} + 2^{n+1} \cdot 2^{(C+D)/\tau-n} - 2^{(C+D)/\tau-n} -$$

$$- 2^{n+1} \cdot 2^{D/\tau} + 2^{D/\tau} + 2^{n+1} \cdot 2^{D/\tau} - 2 \cdot 2^{D/\tau} - 2^{n+1} + 2 =$$

$$2^{(C+D)/\tau} - 2^{D/\tau} = 2^{D/\tau}(2^{C/\tau} - 1).$$

Therefore, for all values of τ, C and D

$$FPC = 2^{D/\tau}(2^{C/\tau} - 1) \qquad (11)$$

APPENDIX 4

A Computer Programme, Giving Several Parameters Relevant in DNA Replication and Cell Division in Bacteria

This is reproduced (in FORTRAN language) on the next page (Fig. 24). A value of 24 minutes is assumed for D. However, it is very simple to alter this, if it is proved not to be correct (putting, for instance, D = C/2 instead of statement 4, if this is the case).

The signs are as presented in the text, except that DG is exchanged for $\triangle$G, GB - for $\bar{G}$, MB - for $\bar{M}$ and GOM - for $\bar{G}/\bar{M}$.

If C is known, a simple modification of this programme can be used to investigate changes in D under different cultural conditions, by exploiting values obtained from $\bar{G}$, $\bar{M}$ and FPC.

```
&FORTRAN;


&TIME;5;;


&LIST;
          WRITE(2,11)
          T=36.
          C=36.
          D=24.
          DO 1 I=1,8
          WRITE(2,12)
          DO 2 J=1,135
          EN=C/T
          HOT=2**EN
          EF=HOT-1.
          DG=((HOT*EN*ALOG(2.)-EF)/EF)*100.
          GB=T*((2.**((C+D)/T))-(2.**(D/T)))/(C*ALOG(2.))
          VB=(2.**((C+D)/T))/(2.*ALOG(2.))
          GOV=GB/VB
          RSF=(2.**(EN+1.)-1.)/EF
          FPC=(2.**(D/T))*(2.**EN-1.)
          WRITE(2,13)T,C,EN,EF,HOT,DG,GB,VB,GOV,RSF,FPC
        2 C=C+1.
          C=36.
        1 T=T+1.
          STOP
       11 FORMAT(15X,43HBACTERIAL DNA REPLICATION AND CELL DIVISION)
       12 FORMAT(1H0,6X,1HT,7X,1HC,4X,2HEN,6X,2HEF,4X,3HHOT,6X,2HDG,6X,2HGB,
         15X,2HMB,3X,3HGOM,3X,3HRSF,4X,3HPFC)
       13 FORMAT(1H ,2F8.3,1F6.3,5F8.3,2F6.3,1F7.3)
          END


&UNLIST;
```

TIME

TIM

FIG. 24. The computer program (Fortran language) used to calculate values of C from experimental results.

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