OLM9.2. Coexistence of two *E. coli* strains on a mixture of two resources

„Size doesn't matter": ecological phenomena can be examined by microbial selection experiments (Feldgarden et al. 2003). Microbial examples are often presented in TBE because of their elegance and simplicity. Experimental results in microbial lab systems tend to be accurate, repeatable and general. This is why these systems provide deep insights into the mechanisms shaping the behaviour of populations and the composition of communities (Jessup et al. 2004). The case of the *lac* operon mutants of *E. coli* competing for substitutable sugar resources introduced in Ch9.2.2 (p.180) will be presented in more detail here. These series of model-based experiments are probably the best experimental studies on the robustness of coexistence of competing reproductive units thus far.

Even though the regulation of lactose metabolism is complicated, the scheme of the sugar uptake process can be substantially simplified for modelling purposes (Figure 9.2.1).

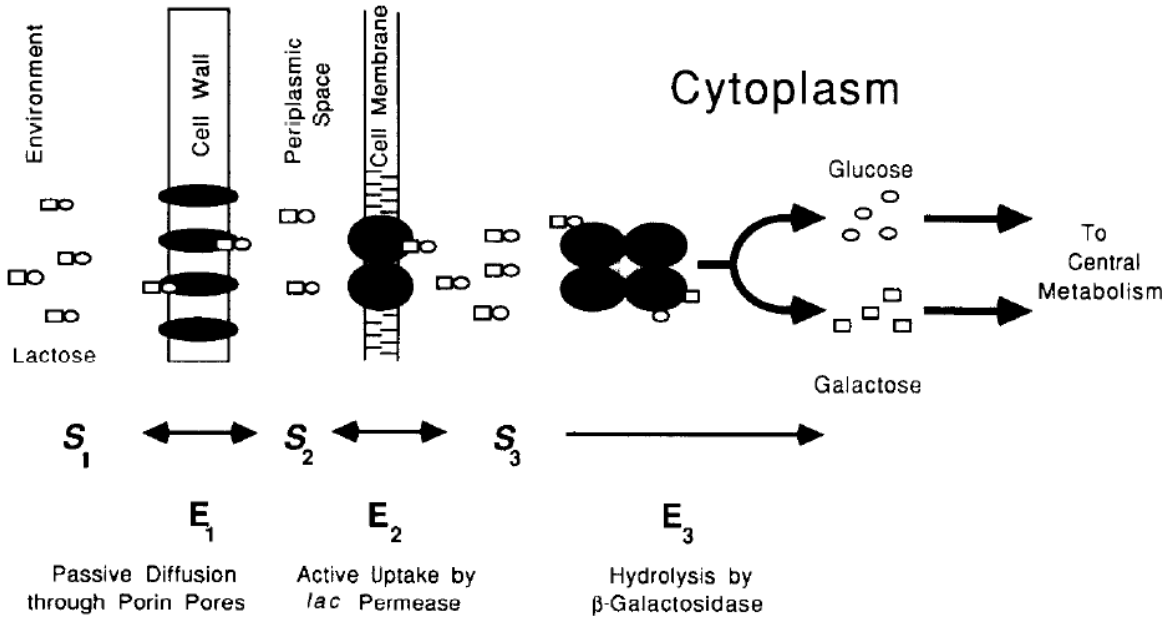

Figure 9.2.1: *E.coli* lactose uptake and metabolism (after Dykhuizen and Dean 1990).

Lactose diffuses (process E_1) from the medium (S_1) through the cell wall into the periplasmic space (S_2). It is transported actively (process E_2) to the cytoplasm (S_3) by lactose permease where it is hydrolysed (E_3) by β-galactosidase to galactose and glucose. This reaction is irreversible.

In this system the metabolic rate depends on the passive diffusion through the cell wall and the kinetics of the two enzymatic reactions. The speed of the lactose metabolism, i.e. the

flux of the metabolites in equilibrium is determined by the speed of the depicted three processes. Modelling the population dynamics can be restricted to them as the hydrolysis of lactose is irreversible thus the downstream reactions do not influence the flux (Dykhuizen & Dean 1990).

In population dynamic equilibrium, when the resource concentration (R) in the environment is low, the two enzymes and the porin pores are unsaturated. The flux of the lactose metabolism can be given as

$$J = \frac{R}{\frac{1}{D_{wall}} + \frac{K_{m.permease.}}{V_{max.permease}} + \frac{K_{m.\beta-gal}}{V_{max.\beta gal} K_{eq.permease}}} \qquad (9.2.1)$$

D_{wall} is the diffusion constant of the porin pores, $K_{m,i}$ and $V_{max,i}$ are parameters of the Michaelis-Menten kinetics of the ith enzymatic process and $K_{eq.permease}$ is an equilibrium constant that characterize the lactose uptake across the cell membrane (Dykhuizen and Dean, 1990; Lunzer et. al. 2002).

It follows from the above argument, that when two potential substrates are provided for an *E.coli* culture their metabolic rates are affected by those mutations that influence the speed of the active uptake of the substrates. Accordingly, the relative fitness of a pair of such mutants must be equal to the relative metabolic flux of the nutrients. Figure 9.2.2 shows that this is the common case.

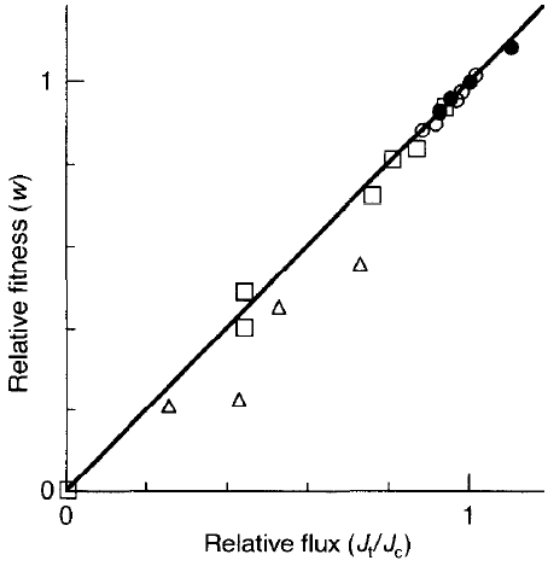

Figure 9.2.2. Relation between the rate of metabolism and relative fitness (Dykhuizen and Dean 1990).

Different types of data points denote results of experiments with different mutant types of the lactose metabolic pathway. The line is the theoretical prediction (relative fitness equals the relative flux).

When the bacteria affect each other only through changing the nutrient concentration in the medium and the two substrates can be considered as perfectly substitutable resources (p.180-182) the relative fitness (TBox7.1, p.123) of the rare type (as measured by the ratio of

the *pgr*s of the two types) is the arithmetic mean fitness weighted by the proportional supply rates of the substrates

$$w_{TD10C} = aw_{TD10C,A} + bw_{TD10C,B} \qquad (9.2.2)$$

or

$$w_{TD2} = aw_{TD2,A} + bw_{TD2,B} \qquad (9.2.3)$$

where TD10C and TD2 are the competing lines, *a* and *b* are the relative frequencies of the two supply rates, and $w_{x,Y}$ is the relative fitness of the *x* strain maintained on pure Y (Y = A or B; lactulose and methyl-galactoside) substrate (Lunzer et al. 2002, Appendix). Since the relative fitness of the common type is the reciprocal of the relative fitness of the rare type, the fitness of the TD10C strain when it is common is

$$w_{\mathrm{TD10C}} = \frac{1}{aw_{\mathrm{TD2,A}} + bw_{\mathrm{TD2,B}}} = \frac{1}{\frac{a}{w_{\mathrm{TD10C,A}}} + \frac{b}{w_{\mathrm{TD10C,B}}}} \qquad (9.2.4)$$

which is the harmonic mean of its relative fitness values measured on pure resources.

The two mutants coexist if the relative fitness of a mutant is larger than 1 when it is rare, thus

$$w_{TD10C} = aw_{TD10C,A} + bw_{TD10C,B} > 1, \qquad (9.2.5)$$

while its relative fitness is smaller than 1 when it is common:

$$w_{\mathrm{TD10C}} = \frac{1}{\frac{a}{w_{\mathrm{TD10C,A}}} + \frac{b}{w_{\mathrm{TD10C,B}}}} < 1. \qquad (9.2.6)$$

These conditions are always met when there is a difference between the relative fitness of the two strains (remember that the arithmetic mean is never smaller than the harmonic mean); however, the difference is small even if the strains are specialised to a large extent to different substrate types (Figure 9.10, p.180). The experimental results confirmed this simplified model as the ratios of the supply rates of those cultures where two strains occurred in stable coexistence all were in the range predicted by Eqs. (9.2.5) and (9.2.6).

Lunzer et. al. (2002) gave a more detailed presentation of the model in the appendix of their paper. Dykhuizen and Dean (2004) studied the robustness of coexistence of these *E.coli* strains in face of new mutations experimentally. Although, they expected that the coexistence will collapse soon due to selective sweep of an advantageous mutant it proved to be quite robust. The molecular background of the trade-off responsible for divergence has to be found.

References

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