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Location of the Maltose A and B Loci on the Genetic Map of *Escherichia coli*[1]

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ABSTRACT

SCHWARTZ, MAXIME (Institut Pasteur, Paris, France). Location of the maltose A and B loci on the genetic map of *Escherichia coli*. J. Bacteriol. **92**:1083–1089. 1966.—All of the mutations impairing maltose metabolism that have been found in *Escherichia coli* map in one of the two loci, *malA* and *malB*. The position of *malA* in relation to the streptomycin, diaminopimelic acid + homoserine, and glycerol D loci were established both by sexual crosses and by P1 transduction. A new biotin marker was also shown to be located in this region. The position of *malB* was studied in relation to the loci for arginine F, methionine A, ultraviolet radiation A, and the origin of transfer of Hfr P10.

The great majority of mutations impairing the metabolism of maltose that have been described in *Escherichia coli* have been shown to map in *mal-A*.

The structural genes for amylomaltase (13, 20) and maltodextrin phosphorylase (16) most probably belong in this region (16). The mutations having the pleiotropic phenotypic expression "maltose minus" and "resistance to phage λ" (10) constitute a third gene of this region, tightly linked with the preceding ones (*unpublished data*).

The *malA* locus is located between *str* and *xyl* (2) and is cotransducible with *str* by phage P1 at a frequency of about 1% the frequency of transduction of *str* or *malA* alone (12).

Two genes, aside from *str*, were recently shown to be cotransducible with *malA*: the structural genes for aspartate semialdehyde dehydrogenase (3; G. N. Cohen and J. C. Patte, *personal communication*) and L-α-glycerophosphate dehydrogenase (N. R. Cozzarelli, *personal communication*). Mutational alteration of the former results in an absolute requirement for both diaminopimelic acid and homoserine, whereas alteration of the latter results in the inability of the mutant to ferment glycerol.

The results presented here give the location of these two genes with relation to *malA* and *str*. The nutritional requirements of mutants having certain kinds of deletions indicate the presence of a "biotin" marker in the *malA* region.

The *malB* locus was first described by Richter (15) under the name of *mal-5*, and was mapped between *thi* and *thr*. The *mal-5*$^-$ mutation he obtained occurred simultaneously with a change from F$^+$ to Hfr; the F factor of this Hfr strain (Hfr-3) could not be dissociated from the *mal*$^-$ mutation by recombination. The phenotypic expression of this mutation is indistinguishable from the pleiotropic mutations found in *malA* (*mal*$^-$ and λ-*r*). I now have found in *malB* other mutations which result in phenotypic expression different from that of *mal-5*$^-$. One of these, MPE1, results both in an impairment of the maltose-concentrating system and a constitutive synthesis of amylomaltase. As such, it is analogous to another mutation that was recently described in the same system (1). In this work, the location of MPE1 in relation to *mal-5*$^-$ has been determined, as well as its location relative to the neighboring genes *argF*, *metA*, *uvrA*, and the origin of transfer of Hfr P10, an Hfr which is shown to be probably analogous to Hfr-3.

MATERIALS AND METHODS

Abbreviations. The following abbreviations are used: *glu*, *mal*, *gly*, and *xyl* correspond to the ability to use, respectively, glucose, maltose, glycerol, and xylose as a carbon source; *thi*, *bio*, *arg*, *met*, *thr*, *leu*, *pro*, *his*, and *ile* correspond to the ability to synthetize thiamine, biotin, L-arginine, L-methionine, L-threonine, L-leucine, L-proline, L-histidine, and L-isoleucine; *dap* + *hom*, ability to synthetize both *meso* (α,ε)-

[1] This work was done in partial fulfillment of the requirements for the degree of "Doctor es Sciences" at the University of Paris.

diaminopimelic acid and L-homoserine; *str-r* and λ-*r*, resistance to streptomycin and bacteriophage λ; *uvr*$^+$, resistance to ultraviolet radiation; *pho* corresponds to the ability to synthetize alkaline phosphatase. The mutations resulting in the inability to synthetize a given amino acid or vitamin, or to use a sugar as a carbon source, are abbreviated by the name of this compound followed by a letter. This letter refers to the genetic location of the mutation according to the nomenclature of Taylor and Thoman (18; Fig. 1).

Media. Broth: 1% peptone (Difco) with 0.5% meat extract (Liebig) and 0.5% NaCl. Tryptone-agar and soft tryptone-agar contained 1% tryptone (Difco), 0.5% yeast extract (Difco), 0.5% NaCl, and, respectively, 1 and 0.6% agar (Difco).

The minimal medium M63 (14) was supplemented with 0.01% of the necessary L-amino acids, 0.0005% thiamine, 0.6% of the sugar used as a carbon source (glucose, maltose, or glycerol), and 1% agar. Streptomycin, when used, was present in concentrations of 0.05%.

The *dap* + *hom* mutants were grown either in broth supplemented with 0.005% diaminopimelic acid (Cyclo) or in minimal medium with 0.05% diaminopimelic acid and, in place of homoserine, 0.01% threonine plus 0.005% methionine. The *bio* mutants were provided with 0.0001% biotin when grown in minimal medium.

Eosin-methylene blue-glycerol medium is EMB medium (11) supplemented with 1.2% glycerol.

Bacteria. The strains of *E. coli* K-12 employed are described in Table 1, together with their origin.

Bacteriophages. Bacteriophage P1kc (12) was used for all transduction experiments. Stocks were made by the plate technique (17) on tryptone-agar plates supplemented with 10^{-3} M $CaCl_2$; they were sterilized with chloroform and kept at 4 C over this material. Strain C600 was used as indicator for titration of the stocks. Phage stocks titering from 5×10^9 to 2×10^{10} phages per milliliter were routinely used.

A virulent mutant of bacteriophage λ was used to select for λ-*r* bacterial mutants. This mutant λV was isolated by Jacob and Wollman (7). The preparation and titering of λV stocks were essentially the same as for P1kc, except that $CaCl_2$ was omitted. The λV stocks were prepared on strain HfrH.

The original stocks of both P1kc and λV came from the collection of F. Jacob.

Transduction and bacterial matings. Transductions by phage P1kc were carried out by incubating phage and bacteria for 3 hr at 25 C with strong agitation in broth supplemented with 10^{-3} M $CaCl_2$. In such transductions, bacteria in exponential phase were used at a concentration of about 5×10^8 per milliliter, and the multiplicity of infection was close to 1.

Matings were carried out in broth according to the method of Jacob and Wollman (9). When necessary, the matings were interrupted by agitation for 1 min in a Vortex Junior mixer after a 10-fold dilution. Recombinants for desired markers were selected on appropriate minimal medium.

Recombinants resistant to ultraviolet irradiation (*uvr*$^+$) were distinguished from the sensitive by irradiating the plates with a dose giving 25% survivors for *uvr*$^+$ bacteria and 0.05% for *uvr*$^-$.

Selection of bacterial mutants resistant to phage λV. Exponentially growing cultures of bacteria containing 5×10^8 cells per milliliter were centrifuged and then suspended in a sterile solution of 10^{-2} M $MgSO_4$. They were starved for 1 hr with agitation at 37 C and were then infected with λV at a multiplicity of infection of about 10. After incubation for 2 hr at 37 C, the suspension was centrifuged again for concentration and plated on EMB-agar with some added λV (about 10^9 per plate). This procedure avoids late-occurring resistant mutants.

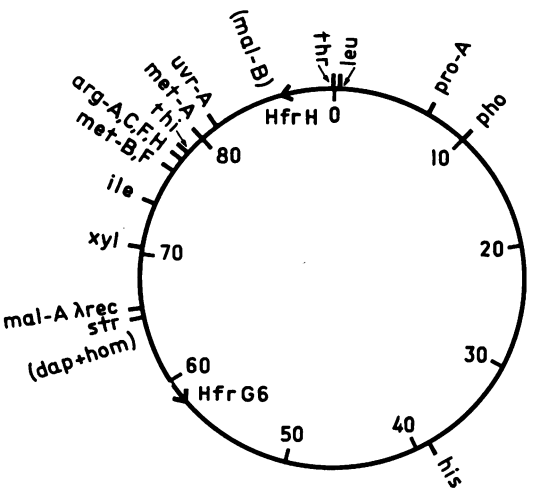

FIG. 1. *Genetic map of Escherichia coli (after A. L. Taylor and M. S. Thoman), giving the location of the different mutations carried by the strains listed in Table 1 or to which reference is made in the text. The map is graduated in 10-minute intervals in terms of chromosome transfer in Hfr × F$^-$ conjugation. The symbol "λrec" stands for "λ receptors." The only addition to the map published by Taylor and Thoman concerns the sites of the origins of transfer of HfrG6 and HfrH.*

RESULTS

Locus malA. The results confirmed the data obtained by others. Locus *malA* was always found distal to *str* with respect to the direction of transfer of HfrG6, and was less than 1% cotransducible with *str* by phage P1. Its cotransducibility with *dap* + *hom* was studied in detail with about 20 different *mal*$^-$ mutants. Scoring of about 8,000 transductants gave a cotransduction index of 60%. Studied with less detail, the cotransduction frequency of *glyD* with *malA* was found to be about 90%. Table 2 illustrates the cotransducibility of these three markers in a particular experimental situation. Loci *glyD* and *dap* + *hom* are thus more closely linked to *malA* than is *str*, and must be on the same side of *str* as *malA*.

The order of the genes *str*, *malA*, and *dap* +

TABLE 1. *Characteristics of the strains used*

Strain	Sex	Characters	Origin
C600	F^-	*thr leu str-s*	F. Jacob
PA505	F^-	*pro his argF metA str-r*	F. Jacob
PA505 MS	F^-	*pro argF metA str-r*	Recombinant, HfrH × PA505
PA505 MS1	F^-	(*dap* + *hom*) *str-r*	Recombinant, HfrH U482 × PA505
PA505 MS7	F^-	(*dap* + *hom*) *glyD*$^-$ *str-r*	Transduction of a *malA*$^-$ derivative of PA505 MS1 by P1/95[a]
PA505 MPE11	F^-	*argF metA malB*$^-$ *str-r*	Recombinant, HfrG6 MPE1 × PA505 MS
PA505 MS9	F^-	*argF metA uvrA*$^-$ *str-r*	Transduction of PA505 MPE11 by P1/KMBL82[a]
KMBL82	F^-	*arg ile uvrA*$^-$ *str-r*	A. Rörsh
KMBL82 MPE1	F^-	*malB*$^-$ *uvrA*$^-$ *str-r*	Recombinant HfrG6 MPE1 × KMBL82
♀ 3.3876.2	F^-	*leu malB*$^-$ *str-r*	A. Richter, F. Jacob, P. Lengyel
HfrH	Hfr	*str-s*	F. Jacob
HfrH U482	Hfr	(*dap* + *hom*) *str-s*	F. Jacob, G. Cohen
HfrH U482 MT18	Hfr	(*dap* + *hom*) *malA*$^-$ *str-s*	Mutant (NTG)[b] of HfrH U482
HfrG6	Hfr	*his str-s*	G. Matney
HfrG6 MPE1	Hfr	*his malB*$^-$ *str-s*	Mutant (ultraviolet) of HfrG6
HfrG6 MT8	Hfr	*his malA*$^-$ *str-s*	Mutant (spontaneous) of HfrG6
Hfr-P10	Hfr	*thr leu str-s*	F. Jacob
95	Hfr	*pho*$^-$ *glyD*$^-$ *str-s*	N. R. Cozzarelli

[a] P1/95 and P1/KMBL82 stand for: phage P1kc lysate obtained, respectively, on strains 95 and KMBL82.

[b] *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine.

TABLE 2. *Ordering of* (*dap* + *hom*), *glyD*, *and malA by a transduction involving three factors*[a]

Genotype of donor	Genotype of acceptor	No. of (*dap* + *hom*)$^+$ recombinants tested	*mal*$^+$ *gly*$^-$	*mal*$^-$ *gly*$^+$	*mal*$^-$ *gly*$^-$	*mal*$^+$ *gly*$^+$
(*dap* + *hom*)$^+$ *glyD*$^-$ *malA*$^+$	(*dap* + *hom*) *glyD*$^+$ *malA*$^-$	305	181	98	23	3

[a] P1 lysate was made on strain 95 as a donor, and the transduction was on HfrH U482 MT18 as an acceptor. Preparation of phage stock and transduction were carried out under standard conditions. The recombinants were isolated before replica plating.

hom was determined as follows: sexual crosses were performed between *str-s* Hfr and *str-r* F^-, the *malA* and *dap* + *hom* loci being distal to *str* with respect to the polarity of chromosome transfer; the selection was devised for recombinants resulting from a crossing over between *malA* and *dap* + *hom*, these being then scored for *str-r* segregation. The results of two such crosses are given in Table 3. As *str* segregates much more frequently with *malA* than with *dap* + *hom*, the order is unequivocally established as *str malA* (*dap* + *hom*).

The *glyD* locus was then mapped in relation to *malA* and *dap* + *hom* by the following three-point test analysis: a *malA*$^-$ (*dap* + *hom*)$^-$ strain was transduced by a P1kc lysate obtained on a *glyD*$^-$ strain. The selection was made for (*dap* + *hom*)$^+$ transductants, these then being scored for glycerol and maltose fermentation.

Only 1.6% of the transductants receiving the *mal*$^+$ character from the donor did not receive the *gly*$^-$ character, whereas 11% of those receiving the *gly*$^-$ character did not receive its *mal*$^+$ character (Table 2). This leads to the conclusion that *glyD* is located between *malA* and *dap* + *hom*.

This location was confirmed by the results (Table 4) of a cross between a *malA*$^-$ HfrG6 and a *glyD*$^-$ (*dap* + *hom*)$^-$ F^- [independent segregation of *gly* and *str* among the *mal*$^+$ (*dap* + *hom*)$^+$ recombinants]. Furthermore, this experiment allows an estimation of the distance between *malA* and *glyD* as being about 40% of the distance between *malA* and *dap* + *hom*.

It has been shown in other systems (21) that a large proportion of spontaneous mutations are multisite mutations. One may then expect to find, among spontaneous *malA*$^-$ mutations, deletions

TABLE 3. *Segregation of str among (dap + hom)$^+$ mal$^+$ recombinants*[a]

Cross	Donor genotype	Acceptor genotype	No. of *str-r* among 100 (*dap* + *hom*)$^+$ *mal*$^+$
HfrH U482 × PA505.....	*str-s malA*$^+$ (*dap* + *hom*)	*str-r malA*$^-$ (*dap* + *hom*)$^+$	3
HfrG6 MT8 × PA505 MS1....	*str-s malA*$^-$ (*dap* + *hom*)$^+$	*str-r malA*$^+$ (*dap* + *hom*)	90

[a] Crosses were carried out under standard mating conditions; mated cultures were plated on minimal maltose-agar. The recombinants of both crosses were isolated before streaking on master plates for replica plating.

TABLE 4. *Segregation of glyD and str among (dap + hom)$^+$ mal$^+$ recombinants*[a]

Donor genotype	Acceptor genotype	No. of (*dap* + *hom*)$^+$ *mal*$^+$ scored	*gly*$^-$		*gly*$^+$	
			Total	*str-r*	Total	*str-r*
str-s (*dap* + *hom*)$^+$ *glyD*$^+$ *malA*$^-$	*str-r* (*dap* + *hom*) *glyD*$^-$ *malA*$^+$	191	118	17	73	18

[a] The cross was carried out under standard mating conditions; mated cultures were plated o n minimal maltose-agar. The donor strain was HfrG6 MT8; the acceptor was PA505 MS7.

which would cover at the same time the *malA* and *glyD* or even the *malA*, *glyD*, and *dap* + *hom* loci. A selection for such types of mutations was devised on the basis of the λ-*r* phenotypic expression of a certain category of *mal*$^-$ mutations. It was done as follows: HfrG6 cultures were grown in diaminopimelic acid-supplemented broth and submitted to a selection for λ-*r* mutants; the λV treated cultures were then plated on diaminopimelic acid-supplemented EMB-glycerol. About 1% of the colonies obtained were small and white, as is usual for *glyD*$^-$ mutants on this medium (4). On reisolation, the majority of them proved to be *mal*$^-$ *gly*$^-$ mutants. Aside from the parental nutritional requirement for histidine, some of these exhibited the additional requirements shown in Table 5. If the *dap* + *hom* requirement of types 1 and 3 may be interpreted as the result of deletions covering the *dap* + *hom* locus studied earlier, the biotin requirement of types 2 and 4 would indicate that some of the deletions cover some locus involved in biotin synthesis. The nature of these mutations is being further studied. As shown in Table 5, both the (*dap* + *hom*)$^+$ and (*dap* + *hom*)$^-$ mutants can be either *bio*$^+$ or *bio*$^-$. Thus, the *bio* locus is not between *malA* and *dap* + *hom* [the totality of the (*dap* + *hom*)$^-$ would then be *bio*$^-$] or between *dap* + *hom* and *xyl* [none of the (*dap* + *hom*)$^+$ would be *bio*$^-$]; it must then be located between *malA* and *str*.

The genetic map of the *malA* region is drawn on approximate scale in Fig. 2, together with the four types of multisite mutants described in Table 5.

TABLE 5. *Nutritional characteristics of spontaneous λ-r gly$^-$ mutants*[a]

Type of mutant	Sugar utilization			Growth factor requirements	
	glu	*gly*	*mal*	(*dap* + *hom*)	*bio*
1	+	−	−	+	+
2	+	−	−	+	−
3	+	−	−	−	+
4	+	−	−	−	−

[a] The nutritional pattern of the mutants was shown by presence or absence of growth after 48 hr at 37 C in the appropriate liquid minimal medium inoculated at a final concentration of 10^5 bacteria per milliliter from a broth culture containing 10^9 bacteria per milliliter.

Locus malB. To study the linkage between the original *mal-5*$^-$ mutation found by Richter and the MPE1 mutation described in the introduction, a sexual cross was performed between a *his* Hfr, HfrG6 MPE1, carrying the MPE1 mutation, and a *leu* F$^-$, ♀ 3.3876.2, carrying the *mal-5*$^-$ mutation. The latter strain is a *leu* mutant obtained from an acridine-cured F$^+$ derivative of Hfr3. Only one *mal*$^+$ was found among 600 *leu*$^+$ *his*$^+$ recombinants tested; this result indicates a close linkage between *mal-5*$^-$ and MPE1. It has since been further confirmed by transduction experiments.

The MPE1 mutation was then used to locate *malB* on the chromosome.

In Table 6 are given the results of a sexual cross between HfrG6 MPE1 (*his malB*$^-$) and

PA505MS (*argF met-A*). As expected, *metA* being distal to *argF* with respect to the polarity of chromosome transfer, the number of arg^+ recombinants was greater among the met^+ than the reverse. The fact that the proportion of met^+ was much higher than the *met* in the arg^+ mal^- shows that *malB* is distal both to *argF* and *metA*. Furthermore, these results indicate that the distance between *metA* and *malB* is of the same order of magnitude as the distance from *argF* to *metA*. Since a previous experiment had shown that *argF* and *metA* were cotransducible at a frequency of about 25% (77 double transductants met^+ arg^+ among 300 met^+), cotransducibility of *malB* and *metA* could also be expected. A *metA* $malB^-$ strain, PA505 MPE11, was transduced to met^+ by a P1 phage grown on a *met* A^+ $malB^+$ strain (HfrH); among 208 met^+ tested, 39 were mal^+. The cotransducibility of the two markers, related to the number of met^+, is thus close to 20%.

Since the locus *uvrA* had already been assigned to this region (6, 19), the linkage of *malB* with *uvrA* was then tested. KMBL82 MPE1 is a strain bearing a $uvrA^-$ mutation, of the hcr^- type (5), and the $malB^-$ mutation MPE1. This strain was transduced to mal^+ by a P1 phage grown on HfrH ($malB^+$ $uvrA^+$). Among 327 mal^+ tested, 223 were found to be uvr^+; the cotransducibility of *malB* and *uvrA* was thus 68% in this experiment.

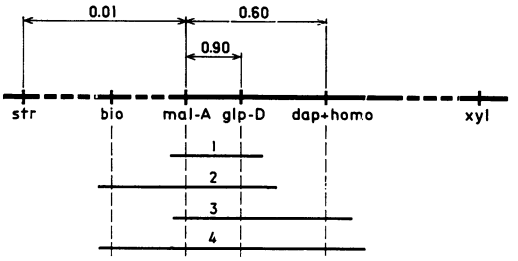

FIG. 2. *Genetic map of the malA region of the Escherichia coli chromosome. The distances are given in cotransduction frequencies (phage P1). The lines under the map represent the extent of the four deletion types listed in Table 5.*

The relative positions of *metA*, *malB*, and *uvrA* were determined by three-point test analysis, both by means of a sexual cross and a P1 transduction (Table 7). In both experiments, met^+ recombinants were selected in crosses between a $metA^+$ $malB^-$ $uvrA^+$ donor and a *metA* $malB^+$ $uvrA^-$ acceptor. In both instances, the class mal^- uvr^- was found to be more numerous than the mal^+ uvr^+, a result which favors the order *metA malB uvrA*.

Studies with Hfr-P10. A series of Hfr strains independently isolated from the same F^+ by Jacob and Wollman (8) inject *argF* and *metB* as early markers. A study of their genealogy shows that they also became mal^- and λ-*r* at the time they became Hfr. This fact suggests that these Hfr strains may be analogous to Richter's Hfr-3. Some results have been obtained with one of them, Hfr-P10, which support this hypothesis (J. Georges, *personal communication*; M. Schwartz, *unpublished data*). The experiments will not be described here, since they are more or less analogous to those of Richter with Hfr-3, but the results can be summarized as follows. (i) The mal^- mutation of Hfr-P10 is in *malB*. It recombines at a high frequency with $malA^-$ mutations and at a low frequency with $malB^-$. (ii) The sex factor of Hfr-P10 is very closely linked with the mal^- mutation of this strain; mal^+ transductants are invariably F^+. (iii) Hfr-P10 is an unstable Hfr. In a cross between Hfr-P10 and an F^- interrupted at 30 min, close to 100% of the F^- cells were converted to F^+.

To locate the origin of transfer of Hfr-P10 relative to the MPE1 mutation, a cross was performed between Hfr-P10 and an *argF metA* F^- carrying the MPE1 mutation, PA 505 MPE11, and the mating was interrupted at 30 min. Under such conditions, it was observed that $metA^+$ and

TABLE 6. *Ordering of argF, metA, and malB by sexual cross*[a]

Genotype of donor	Genotype of acceptor	Selected character	Unselected character (%)			
			arg^+	met^+	mal^-	
					Total	met^+
$argF^+$ $metA^+$ $malB^-$ *his*	*argF metA* $malB^+$ his^+	arg^+ his^+	—	76	54	53
		met^+ his^+	96	—	78	—

[a] The cross was carried out under standard mating conditions; mated cultures were plated on minimal glucose-agar supplemented with methionine or arginine. The donor strain was HfrG6 MPE1, and the acceptor was PA505 MS; 100 recombinants of each type were scored for unselected markers.

TABLE 7. *Ordering of metA, malB, and uvrA by three-factor crosses*[a]

Type of cross	No. of *met*$^+$ recombinants scored	*mal*$^-$ *uvr*$^+$	*mal*$^+$ *uvr*$^-$	*mal*$^-$ *uvr*$^-$	*mal*$^+$ *uvr*$^+$
Sexual.....	550	226	105	25	6
P1 transduction.....	300	6	278	15	1

[a] Sexual cross and P1 transduction were carried out under standard conditions, and the culture was plated on minimal glucose supplemented with arginine. In both, the donor was HfrG6 MPE1 (*malB*$^-$ *his metA*$^+$ *uvrA*$^+$) and the acceptor was PA505 MS9 (*malB*$^+$ *his*$^+$ *metA uvrA*$^-$). In the sexual cross, the donor was counterselected by its requirement for *his*. The replica plating was on two minimal glucose and two minimal maltose plates. One of each minimal agar plate was irradiated with ultraviolet light.

argF$^+$ were transferred at a very high frequency (the number of recombinants being about 10% of the number of Hfr), whereas *mal*$^+$ recombinants appeared at a frequency about 5×10^{-3} times lower. These *mal*$^+$ recombinants could have arisen either from a late transfer of the wild-type allele of MPE1 followed by a recombination between the *mal*$^-$ mutations of the two parents, or by an early transfer of this locus, the frequency of integration being very low as a consequence of the close linkage between MPE1 and the origin of transfer of the Hfr. Evidence supporting the second hypothesis was given by the results of crosses between Hfr-P10 and two *uvrA*$^-$ F$^-$, KMBL82 MPE1 and PA505 MS9. Among 300 *mal*$^+$ *str-r* recombinants obtained in a cross between Hfr-P10 and KMBL82 MPE1 (which carries the MPE1 mutation), none was found to be *uvr*$^+$. Similarly, in the cross with the *metA argF* F$^-$, PA505 MS9, no *uvr*$^+$ was found among 200 *arg*$^+$ *met*$^+$ *str-r*.

If MPE1 were a distal marker, *metA* and *argF* being proximal ones, one would expect a high proportion of *uvr*$^+$ in the *mal*$^+$ recombinants of the first cross and a low proportion in the *arg*$^+$ *met*$^+$ of the second. The fact that this proportion was low (not detectable in these experiments) in both cases is taken as evidence for the wild-type allele of MPE1 being an early marker of Hfr-P10. In Fig. 3, the results obtained on the *malB* region of the genetic map are summarized.

DISCUSSION

All of the *mal*$^-$ mutations that have been mapped on the *E. coli* chromosome were shown to be located in one of the two loci, *malA* and *malB*. The *malA* and *malB* mutations can be distinguished from one another by cotransduction with (*dap* + *hom*) and *glyD* or with *metA* and *uvrA*, respectively.

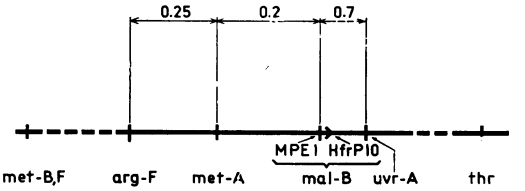

FIG. 3. *Genetic map of the malB region of the Escherichia coli chromosome. The distances are given in cotransduction frequencies (phage P1). MPE1 is a malB*$^-$ *mutation. HfrP10 is a malB*$^-$ *Hfr whose mal*$^-$ *mutation is not dissociable from the integrated sex factor by recombination.*

The structural genes for amylomaltase and maltodextrin phosphorylase are most probably located in *malA*. The function of the gene, also located in *malA*, whose alteration results in the abolition both of all the enzymatic activities of the system (20) and of the ability to synthesize functional receptors for bacteriophage λ, is not well understood at present. The functions of the genes found in *malB* are also unclear, in particular the one whose alteration gives rise to the MPE1 phenotype, i.e., an impaired maltose-concentrating mechanism, associated with a constitutive synthesis of amylomaltase and maltodextrin phosphorylase. The regulation of the metabolic pathway of maltose in *E. coli* thus seems to show rather complicated features, probably involving some kind of reciprocal interactions between the two loci. The elucidation of the genetic fine structure of these two loci, rendered possible by the results presented here, should throw some light on the problem.

The finding that a number of independently isolated Hfr strains seem to have exactly the same properties as Richter's Hfr-3 suggests that there most probably exists, inside the *malB* locus, a region of high affinity for the F factor.

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LITERATURE CITED

1. BURGER, M., AND E. PAVLASOVA. 1964. Change in the location of amylomaltase produced by mutation in *E. coli*. Biochem. J. 93:601–606.

2. CAVALLI, L. L., J. LEDERBERG, AND E. M. LEDERBERG. 1953. An infective factor controlling sex compatibility in Bacterium coli. J. Gen. Microbiol. **8**:89–103.
3. COHEN, G. N., J. C. PATTE, P. TRUFFA-BACHI, C. SAWAS, AND M. DOUDOROFF. 1965. Repression and end-product inhibition in a branched biosynthetic pathway, p. 243–253. *In* Mécanismes de régulation des activités cellulaires chez les microorganismes. Colloq. Intern. Centre Natl. Rech. Sci. Marseille, 1963.
4. COZZARELLI, N. R., J. P. KOCH, S. HAYASHI, AND E. C. C. LIN. 1965. Growth stasis by accumulated L-α-glycerophosphate in *Escherichia coli*. J. Bacteriol. **90**:1325–1329.
5. HILL, R. F., AND R. R. FEINER. 1963. Further studies of ultra violet-sensitive mutants of *Escherichia coli* strain B. J. Gen. Microbiol. **35**:105–114.
6. HOWARD-FLANDERS, P., R. P. BOYCE, E. SIMSON, AND L. THERIOT. 1962. A genetic locus in *Escherichia coli* K12 that controls the reactivation of uv-photoproducts associated with thymine in DNA. Proc. Natl. Acad. Sci. U.S. **48**:2109–2115.
7. JACOB, F., AND E. L. WOLLMAN. 1954. Étude génétique d'un bactériophage tempéré d'*Escherichia coli*. Ann. Inst. Pasteur **87**:653–674.
8. JACOB, F., AND E. L. WOLLMAN. 1957. Analyse des groupes de liaison génétique de différentes souches donatrices d'*E. coli* K12. Compt. Rend. **245**:1840–1843.
9. JACOB, F., AND E. L. WOLLMAN. 1961. Sexuality and the genetics of bacteria, p. 63. Academic Press, Inc., New York.
10. LEDERBERG, E. M. 1955. Pleiotropy for maltose fermentation and phage resistance in *E. coli* K12. Genetics **40**:580–581.
11. LEDERBERG, J. 1947. Gene recombination and linked segregation in *Escherichia coli*. Genetics **32**:505–525.
12. LENNOX, E. S. 1955. Transduction of linked genetic characters of the host by bacteriophage P1. Virology **1**:190–206.
13. MONOD, J., AND A. M. TORRIANI. 1950. De l'amylomaltase d'*Escherichia coli*. Ann. Inst. Pasteur **78**:65–77.
14. PARDEE, A. B., F. JACOB, AND J. MONOD. 1959. The genetic control and cytoplasmic expression of "inducibility" in the synthesis of β-galactosidase by *E. coli*. J. Mol. Biol. **1**:165–178.
15. RICHTER, A. 1961. Attachment of wild type F factor to a specific chromosomal region in a variant strain of *E. coli* K12: the phenomenon of episomic alternation. Genet. Res. **2**:333–345.
16. SCHWARTZ, M. 1965. Aspects biochimiques et génétiques du métabolisme du maltose chez *Escherichia coli* K12. Compt. Rend. **260**:2613–2616
17. SWANSTROM, M., AND M. H. ADAMS. 1951. Agar layer method for production of high titer phage stocks. Proc. Soc. Exptl. Biol. Med. **78**:372–375.
18. TAYLOR, A. L., AND M. S. THOMAN. 1964. The genetic map of *Escherichia coli* K12. Genetics **50**:659–677.
19. VAN DE PUTTE, P., C. A. VAN SLUIS, J. VAN DILLEWIJN, AND A. RÖRSCH. 1965. The location of genes controlling radiation sensitivity in *E. coli*. Mutation Res. **2**:97–110.
20. WIESMEYER, H., AND M. COHN. 1960. The characterization of the pathway of maltose utilization by *Escherichia coli*. Biochim. Biophys. Acta **39**:417–447.
21. YANOFSKY, C., AND E. S. LENNOX. 1959. Transduction and recombination study of linkage relationships among the genes controlling tryptophan synthesis in *Escherichia coli*. Virology **8**:425–447.