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# Compilation and analysis of *Escherichia coli* promoter DNA sequences

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## ABSTRACT

The DNA sequence of 168 promoter regions (-50 to +10) for Escherichia coli RNA polymerase were compiled. The complete listing was divided into two groups depending upon whether or not the promoter had been defined by genetic (promoter mutations) or biochemical (5' end determination) criteria. A consensus promoter sequence based on homologies among 112 well-defined promoters was determined that was in substantial agreement with previous compilations. In addition, we have tabulated 98 promoter mutations. Nearly all of the altered base pairs in the mutants conform to the following general rule: down-mutations decrease homology and up-mutations increase homology to the consensus sequence.

## INTRODUCTION

Promoters for Escherichia coli RNA polymerase have been shown to contain two regions of conserved DNA sequence, located about 10 and 35 base pairs upstream of the transcription startsite (75,107,112,204). Although promoters are expected to share common structural features reflecting a similar interaction with RNA polymerase, comparison of promoter sequences has also revealed considerable sequence diversity. This diversity is related both to the wide range of initiation frequencies and to the partial overlap of binding sites for transcriptional control proteins. In this paper, we have analyzed the sequence homologies among 112 well-defined promoters. We have also tabulated the locations of 98 promoter mutations. This information supports the importance to promoter function of the conserved sequence elements proposed by Rosenberg and Court (205) and Siebenlist et al. (206).

| | TTGACA | TATAAT | +1 | I | II | III |
|---|---|---|---|---|---|---|
| BACTERIAL PROMOTERS | | | | | | |
| araBAD | TTAGCGGATCCTACCTGACGCTTTT | TATCGCAACTCTCTACTGTTTCTCCATACCCGTTTTT | | 1,2 | 3 | |
| araC | GCAAATAATCAATGTGGACTTTTCT | GCCGTGATTATAGACACTTTTGTTACGCGTTTTTGT | | 2,4 | 4 | 4 |
| galP1 | CTAATTTATTCCATGTCACACTTTTCGCATCTTTGTTATGCTATGGTTAT | | TTCATACCATAAG | 5 | 6 | 7 |
| galP2 | CACTAATTTATTCCATGTCACACTT | TTCGCATCTTTGTTATGCTATG | GTTATTTCATACC | 5 | 6 | 7 |
| lacP1 | TAGGCACCCCAGGCTTTACACTTTA | TGCTTCCGGCTCGTATGTTGTG | TGGAATTGTGAGC | 8 | 9 | |
| lacP2 | TTAATGTGAGTTAGCTCACTCATTA | GGCACCCCAGGCTTTACACTTTA | TGCTTCCGGCTCG | 8 | 10,195 | |
| lacI | GACACCATCGAATGGCGCAAAACCT | TTCGCGGTATGGCATGATAGC | GCCCGGAAGAGAGT | 11 | 12 | |
| malEFG | AGGGGCAAGGAGGATGGAAAGAGGT | TGCCGTATAAAGAAACTAGA | GTCCGTTTAGGTGT | 13 | | 14 |
| malK | CAGGGGGTGGAGGATTTAAGCCATC | TCCTGATGACGCATAGTCAG | CCCATCATGAATG | 13 | | 14 |
| malT | AAAAACGTCATCGCTTGCATTAGAA | AGGTTTCTGGCCGACCTTATA | ACCATTAATTACG | 15 | | 16 |
| tnaA | AAACAATTTCAGAATAGACAAAAAC | TCTGAGTGTAATAATGTAGC | CTCGTGTCTTGCG | 17 | 18 | |
| deoP1 | CAGAAACGTTTTATTCGAACATCGA | TCTCGTCTTGTGTTAGAATTCT | AACATACGGTTGC | 19 | 19 | 19 |
| deoP2 | AATTGTGATGTGTATCGAAGTGTGT | TGCGGAGTAGATGTTAGAATACT | AACAAACTCGCAA | 19 | 19 | 19 |
| trp | TCTGAAATGAGCTGTTGACAATTAA | TCATCGAACTAGTTAACTAGT | ACGCAAGTTCACGT | 20 | 21 | 21 |
| trpR | TGGGGACGTCGTTACTGATCCGCAC | GTTTATGATATGCTATCGTACT | CTTTAGCGAGTACA | 22,23 | 22 | |
| aroH | GTACTAGAGAACTAGTGCATTAGCT | TATTTTTTTGTTATCATGCT | AACCACCCGGCGAG | 24 | 24 | |
| trpP2 | ACCGGAAGAAAACCGTGACATTTTA | ACACGTTTGTTACAAGGTAAA | GGCGACGCCGCCC | 25 | 26 | |
| his | ATATAAAAAAGTTCTTGCTTTCTAA | CGTGAAAGTGGTTTAGGTTAAA | AGACATCAGTTGAA | 27 | 28 | 28 |
| hisA | GATCTACAAACTAATTAATAAATAG | TTAATTAACGCTCATCATTGTACA | ATGAACTGTACAAA | 27 | 28 | |
| leu | GTTGACATCCGT | TTTTGTATCCAGTAACTCTAA | AAGCATATCGCATT | 29 | | |
| ilvGEDA | GGCCAAAAAATATCTTGTACTATTT | ACAAAACCTATGGTAACTCTTT | AGGCATTCCTTCGA | 31,32 | 33 | |
| argCBH | TTTGTTTTTCATTGTTGACACACCT | CTGGTCATGATAGTATCAATATTCATGCAGTATT | | 34 | | 34 |
| thr | AAATTAAAATTTTATTGACTTAGGT | CACTAAATACTTTAACCAATATAGGCATAGCGCACA | | 35 | 35 | |
| bioA | GCCTTCTCCAAAACGTGTTTTTTGT | TGTTAATTCGGTGTAGACTTGT | AAACCTAAATCT | 36,37 | 36 | |
| bioB | TTGTCATAATCGACTTGTAAACCAA | ATTGAAAAGATTTAGGTTTACAAGTCTACACCGAAT | | 36 | 36 | |
| fol | CATCCTCGCACCAGTCGACGACGGT | TTACGCTTTACGTATAGTGGC | GACAATTTTTTTT | 38 | | |
| uvrB P1 | TCCAGTATAATTTGTTGGCATAATT | AAGTACGACGAGTAAAATTAC | ATACCTGCCCGC | 39,40 | 40 | |
| uvrB P2 | TCAGAAATATTATGGTGATGAACTG | TTTTTTTATCCAGTATAATTTG | TTGGCATAATTAA | 39,40 | 40 | |
| uvrB P3 | ACAGTTATCCACTATTCCTGTGGAT | AACCATGTGTATTAGAGTTAG | AAAACACGAGGCA | 40 | 40 | |
| recA | TTTCTACAAAACACTTGATACTGTA | TGAGCATACAGTATAATTGC | TTCAACAGAACAT | 41,42 | 41 | |
| lexA | TGTGCAGTTTATGGTTCCAAAATCG | CCTTTTGCTGTATATACTCAC | AGCATAACTGTAT | 43,44 | 43,44 | |
| ampC | TGCTATCCTGACAGTTGTCACGCTG | ATTGGTGTCGTTACAATCTA | ACGCATCGCCAATG | 45 | 45 | |
| lpp | CCATCAAAAAAATATTCTCAACATA | AAAAACTTTGTGTAATACTTGT | AACGCTACATGGA | 46 | | 47 |
| hisJ (S.t.) | CAAGGTAGAATGCTTTGCCTTGTCG | GCCTGATTAATGGCACGATAGT | CGCATCGGATCTG | 48 | | |
| Pori-r | GATCGCACGATCTGTATACTTATTT | GAGTAAATTAACCCACGATCCC | AGCCATTCTTCTGC | 49 | 49 | |
| Pori-l | CTGTTGTTCAGTTTTTGAGTTGTGT | ATAACCCCTCATTCTGATCCC | AGCTTATACGGT | 49 | 49 | |
| spot 42 RNA | ATTACAAAAAGTGCTTTCTGAACTG | AACAAAAAAGAGTAAAGTTAG | TCGCGTAGGGTACA | 50 | | 51 |
| M1 RNA | ATGCGCAACGCGGGGTGACAAGGGC | GCGCAAACCCTCTATACTGCG | CGCCGAAGCTGACC | 52 | | |
| alaS | AACGCATACGGTATTTTACCTTCCC | AGTCAAGAAAACTTATCTTATT | CCCACTTTTCAGT | 53 | 53 | |
| trpS | CTACGGCGAGGCTATCGATCTCAGC | CAGCCTGATGTAATTTATCAGTCTATAAATGACC | | 54 | 54 | 54 |
| glnS | TAAAAAACTAACAGTTGTCAGCCTG | TCCCGCTTATAAGATCATACG | CCGTTATACGTT | 55 | 55 | |

| | | | | | |
|---|---|---|---|---|---|
| tufB | ATGCAATTTTTTAGTTGCATGAACT | CGCATGTCTCCATAGAATGCG | CGCTACTTGATGCC | 56 | 57 | |
| tyrT | TCTCAACGTAACACTTTACAGCGGC | GCGTCATTTGATATGATGCG | CCCCGCTTCCCGAT | 58 | | 59 |
| leu1 tRNA | TCGATAATTAACTATTGACGAAAAG | CTGAAAACCACTAGAATGCGCCTCCGTGGTAGCAA | | 60 | 60 | |
| supB-E | CCTTGAAAAAGAGGTTGACGCTGCA | AGGCTCTATACGCATAATGCG | CCCCGCAACGCCGA | 61 | 62 | |
| rrnAB P1 | TTTTAAATTTCCTCTTGTCAGGCCG | GAATAACTCCCTATAATGCGCCACCACTGACACGG | | 63-64b | 65 | |
| rrnG P1 | TTTATATTTTTCGCTTGTCAGGCCG | GAATAACTCCCTATAATGCGCCACCACTGACACGG | | 66 | | |
| rrnD P1 | GATCAAAAAAATACTTGTGCAAAAA | ATTGGGATCCCTATAATGCGCCTCCGTTGAGACGA | | 67 | 67 | |
| rrnE P1 | CTGCAATTTTTCTATTGCGGCCTGC | GGAGAACTCCCTATAATGCGCCTCCATCGACACGG | | 63 | 65 | |
| rrnX P1 | ATGCATTTTTCCGCTTGTCTTCCTG | AGCCGACTCCCTATAATGCGCCTCCATCGACACGG | | 67 | 67 | |
| rrnAB P2 | GCAAAAATAAATGCTTGACTCTGTA | GCGGGAAGGCGTATTATGCA | CACCCCGCGCCGC | 63-64b | 65 | |
| rrnG P2 | AAGCAAAGAAATGCTTGACTCTGTA | GCGGGAAGGCGTATTATGCA | CACCGCCGCGCCG | 66 | | |
| rrnDEX P2 | CCTGAAATTCAGGGTTGACTCTGAA | AGAGGAAAGCGTAATATACG | CCACCTCGCGACAG | 63,67 | 65,67 | |
| str | TCGTTGTATATTTCTTGACACCTTT | TCGGCATCGCCCTAAAATTCG | GCGTCCTCATAT | 68 | 68 | 69 |
| spc | CCGTTTATTTTTTCTACCCATATCC | TTGAAGCGGTGTTATAATGCC | GCGCCCTCGATA | 68 | 68 | 69 |
| S10 | TACTAGCAATACGCTTGCGTTCGGT | GGTTAAGTATGTATAATGCG | CGGGCTTGTCGT | 70 | | 70 |
| rpoA | TTCGCATATTTTTCTTGCAAAGTTG | GGTTGAGCTGGCTAGATTAGC | CAGCCAATCTTT | 71 | 71 | |
| rplJ | TGTAAACTAATGCCTTTACGTGGGC | GGTGATTTTGTCTACAATCTT | ACCCCCACGTATA | 72 | 72 | |
| rpoB | CGACTTAATATACTGCGACAGGACG | TCCGTTCTGTGTAAATCGCA | ATGAAATGGTTTAA | 72,73 | | |
| | | | | | | |
| PHAGE PROMOTERS | | | | | | |
| T7 A1 | TATCAAAAAGAGTATTGACTTAAAG | TCTAACCTATAGGATACTTAC | AGCCATCGAGAGGG | 74 | 74 | |
| T7 A2 | ACGAAAAACAGGTATTGACAACATG | AAGTAACATGCAGTAAGATACA | AATCGCTAGGTAAC | 74 | 75 | |
| T7 A3 | GTGAAACAAAACGGTTGACAACATG | AAGTAAACACGGTACGATGTA | CCACATGAAACGAC | 74 | 75 | |
| T7 C | CATTGATAAGCAACTTGACGCAATG | TTAATGGGCTGATAGTCTTAT | CTTACAGGTCATC | 76 | 76 | |
| T7 D | CTTTAAGATAGGCGTTGACTTGATG | GGTCTTTAGGTGTAGGCTTTA | GGTGTTGGCTTTA | 77 | 78 | |
| λPR | TAACACCGTGCGTGTTGACTATTTT | ACCTCTGGCGGTGATAATGGT | TGCATGTACTAAG | 79,80 | 81 | |
| λPRM | AACACGCACGGTGTTAGATATTTAT | CCCTTGCGGTGATAGATTTAA | CGTATGAGCACAA | 82,83 | 83,84 | |
| λPL | TATCTCTGGCGGTGTTGACATAAAT | ACCACTGGCGGTGATACTGAG | CACATCAGCAGGA | 85 | 86 | |
| λPo | TACCTCTGCCGAAGTTGAGTATTTT | TGCTGTATTTGTCATAATGAC | TCCTGTTGATAGAT | 87 | 81 | |
| λPR' | TTAACGGCATGATATTGACTTATTG | AATAAAATTGGGTAAATTTGA | CTCAACGATGGGTT | 88 | 89 | |
| λPRE | TAGAGCCTCGTTGCGTTTGTTTGCA | CGAACCATATGTAAGTATTTC | CTTAGATAACAAT | 90 | 91 | |
| λPI | CGGTTTTTTCTTGCGTGTAATTGCG | GAGACTTTGCGATGTACTTGA | CACTTCAGGAGTG | 92-94 | 95 | |
| 434 PR | AAGAAAAACTGTATTTGACAAACAA | GATACATTGTATGAAAATACAAGAAAGTTTGTTGAT | | 96,97 | 97 | |
| 434 PRM | ACAATGTATCTTGTTTGTCAAATAC | AGTTTTTCTTGTGAAGATTGG | GGGTAAATAACAGA | 96,97 | | |
| P22 PR | CATCTTAAATAAACTTGACTAAAGA | TTCCTTTAGTAGATAATTTA | AGTGTTCTTTAAT | 98 | 99 | |
| P22 PRM | AAATTATCTACTAAAGGAATCTTTA | GTCAAGTTTATTTAAGATGAC | TTAACTATGAAT | 98 | 99 | |
| P22 ant | TCCAAGTTAGTGTATTGACATGATA | GAAGCACTCTACTATATTCTC | AATAGGTCCACGG | 100,101 | 102 | |
| P22 mnt | CCACCGTGGACCTATTGAGAATATA | GTAGAGTGCTTCTATCATGTC | AATACACTAACTT | 100,101 | 102 | |
| ΦX A | AATAACCGTCAGGATTGACACCCTC | CCAATTGTATGTTTTCATGCC | TCCAAATCTTGGA | 103 | 104,105 | |
| ΦX D | TAGAGATTCTCTTGTTGACATTTTA | AAAGAGCGTGGATTACTATCTGAGTCCGATGCTGTTC | | 103 | 104 | |
| ΦX B | GCCAGTTAAATAGCTTGCAAAATAC | GTGGCCTTATGGTTACAGTATG | CCCATCGCAGTT | 103,106 | 104,105 | |
| fd VIII | GATACAAATCTCCGTTGTACTTTGT | TTCGCGCTTGGTATAATCGC | TGGGGGTCAAAG | 107-110 | 113,114 | 115 |
| fd X | TCCTCTTAATCTTTTTGATGCAATT | CGCTTTGCTTCTGACTATAATAGA | CAGGGTAAAGACCT | 108-112 | 116 | |

| | | | | | |
|---|---|---|---|---|---|
| PLASMID & TRANSPOSON PROMOTERS | | | | | |
| pBR322 bla | TTTTTCTAAATACATTCAAATATGT | ATCCGCTCATGAGACAATAAC | CCTGATAAATGCT | 117 | 118,119 |
| pBR tet | AAGAATTCTCATGTTTGACAGCTTA | TCATCGATAAGCTTTAATGCG | GTAGTTTATCACA | 120 | 121 121 |
| pBR P1 | TTCATACACGGTGCCTGACTGCGTTAGCAATTTAACTGTGATAAACTACC | | GCATTAAAGCTTA | 120 | 121 121 |
| pBR RNAI | GTGCTACAGAGTTCTTGAAGTGGTG | GCCTAACTACGGCTACACTAGA | AGGACAGTATTTG | 120 | 122,123 |
| pBR primer | ATCAAAGGATCTTCTTGAGATCCTT | TTTTTCTGCGCGTAATCTGCT | GCTTGCAAACAAAA | 120 | 118 |
| pBR322 P4 | CATCTGTGCGGTATTTCACACCGCATATGGTGCACTCTCAGTACAATCTG | | CTCTGATGCCGCAT | 124 | 124 |
| ColE1 P1 | GGAAGTCCACAGTCTTGACAGGGAA | AATGCAGCGGCGTAGCTTTTA | TGCTGTATATAAAA | 125 | 125 |
| ColE1 P2 | TTATTTTTAACTTATTGTTTTAAAA | GTCAAAGAGGATTTTATAATGGA | AACCGCGGTAGCGT | 125 | 125 |
| RSF primer | GGAATAGCTGTTCGTTGACTTGATA | GACCGATTGATTCATCATCTC | ATAAATAAAGAA | 126 | 126 |
| RSF RNAI | TAGAGGAGTTTGTCTTGAAGTTATG | CACCTGTTAAGGCTAAACTGAA | AGAACAGATTTTG | 126 | 126 |
| CloDF RNAI | ACACGCGGTTGCTCTTGAAGTGTGC | GCCAAAGTCCGGCTACACTGGA | AGGACAGATTTGG | 127 | 127 |
| R100 RNAI | CACAGAAAGAAGTCTTGAACTTTTC | CGGGCATATAACTATACTCCC | CGCATAGCTGAAT | 128 | 128 |
| R100 RNAII | ATGGGCTTACATTCTTGAGTGTTCA | GAAGATTAGTGCTAGATTACT | GATCGTTTAAGGAA | 128 | 128 |
| R1 RNAII | ACTAAAGTAAAGACTTTACTTTGTG | GCGTAGCATGCTAGATTACT | GATCGTTTAAGGAA | 128 | 128 |
| R100RNAIII | GTACCGGCTTACGCCGGGCTTCGGC | GGTTTTACTCCTGTATCATATG | AAACAACAGAG | 128 | 128 |
| cat | ACGTTGATCGGCACGTAAGAGGTTC | CAACTTTCACCATAATGAA | ATAAGATCACTACC | 130 | 131 |
| Tn10 Pin | TCATTAAGTTAAGGTGGATACACAT | CTTGTCATATGATCAAATGGT | TTCGCGAAAAATC | 132 | 133 |
| Tn10 Pout | AGTGTAATTCGGGGCAGAATTGGTA | AAGAGAGTCGTGTAAAATATC | GAGTTCGCACATC | 132 | 133 |
| Tn10 tetA | ATTCCTAATTTTTGTTGACACTCTA | TCATTGATAGAGTTATTTTACC | ACTCCCTATCAGT | 134 | |
| Tn10 tetR | TATTCATTTCACTTTTCTCTATCAC | TGATAGGGAGTGGTAAAATAAC | TCTATCAATGATA | 134 | |
| γδ tnpA | ACACATTAACAGCACTGTTTTTATG | TGTGCGATAATTTATAATATT | TCGGACGGTTGCA | 135 | 135 |
| γδ tnpR | ATTCATTAACAATTTTGCAACCGTC | CGAAATATTATAAATTATC | GCACACATAAAAAC | 135 | 135 |
| Tn5 IR | TCCAGGATCTGATCTTCCATGTGAC | CTCCTAACATGGTAACGTTCA | TGATAACTTCTGCT | 136,137 | 138 |
| Tn5 neo | CAAGCGAACCGGAATTGCCAGCTGG | GGCGCCCTCTGGTAAGGTTGG | GAAGCCCTGCAA | 139 | |
| PROMOTERS CREATED BY FUSION OR MUTATION | | | | | |
| lacP115 | TTTACACTTTATGCTTCCGGCTCGT | ATGTTGTGTGGTATTGTGAG | CGGATAACAATTT | 138 | |
| bioP98 | TTGTTAATTCGGTGTAGACTTGTAA | ACCTAAATCTTTTAAATTTGG | TTTACAAGTCGAT | 36 | 36 |
| λc17 | GGTGTATGCATTTATTTGCATACAT | TCAATCAATTGTTATAATTGT | TATCTAAGGAAAT | 90 | 90 |
| λcin | TAGATAACAATTGATTGAATGTATG | CAAATAAATGCATACACTATA | GGTGTGGTTTAAT | 90 | 141 |
| λL57 | TTGATAAGCAATGCTTTTTTATAAT | GCCAACTTAGTATAAAATAGC | CAACCTGTTCGACA | 64 | 142 |
| IS2 I-II | ATGTCTGGAAATATAG | GGGCAAATCCACTAGTATTAA | GACTATCACTTATT | 143 | 143 |

SEQUENCE HOMOLOGIES

We have used biochemical and genetic evidence to decide whether a DNA sequence should be included in our list of promoters. The 112 promoters in Figure 1 were defined by one or both of the following criteria: (i) The 5′ terminal nucleotides of the transcript have been determined, or (ii) one or more promoter mutations have been sequenced. Promoters have also been located less precisely by other techniques, including the measurement of run-off transcript lengths *in vitro*, S1 mapping of an RNA isolated *in vivo*, or detection of an RNA polymerase-DNA complex by filterbinding, protection from enzymatic digestion, or electron microscopy. All of these methods are useful for localizing a promoter to a limited region of DNA; however, the assumption that the promoter can then be more precisely located by finding the best match to a consensus sequence within such a region has proven unreliable. For this reason, those promoters for which the more stringent biochemical or genetic information is unavailable are listed separately in Figure 2. These proposed promoters have not been included in the analysis of sequence homologies.

The separation of promoter sequences into two categories is based on reasonable criteria, but we realize that making such a distinction is not without difficulties. One could argue that several of the proposed promoters in Figure 2 have, in fact, been located precisely by a combination of indirect evidence. For example, some of the fd promoters listed in Figure 2 have been characterized by filter-binding techniques, run-off

Figure 1. Promoters for *E. coli* RNA polymerase. The sense strand sequences of 112 promoters were aligned as described in the text. The consensus sequences for the -35 and -10 region hexamers are shown. The nucleotide corresponding to the major 5′ end of the transcript (+1) is underlined; a dashed line indicates that the RNA was sequenced, and the 5′ end occurs at one or more of the underlined bases. The numbers in the three columns at the right correspond to the references for the DNA sequence (column I), and the 5′ end of the RNA synthesized *in vitro* (II) and *in vivo* (III). The promoters are grouped into four categories: bacterial, phage, plasmid and transposon promoters, and promoters created by mutation. All of the bacterial promoters are from *E coli* K12, except for one *S. typhimurium* promoter (hisJ) that has no sequenced *E. coli* counterpart. Several *S. typhimurium* plasmid and phage promoters were also included. These have been shown to function as promoters in *E. coli*. The DNA from the filamentous phages fd, M13, and f1 have all been sequenced in their entirety. Although only the fd promoters are listed here and in Figure 2, references are given for the DNA sequences of the other two phage genomes.

| | TTGACA | TATAAT | | References |
|---|---|---|---|---|
| araFG | ACTGGAAAGTACGTTTGCAGTGAAA | TAACTATTCAGCAGGATAAT | GAATACAGAGGGGCG | 144,145 |
| malP | TAATCCCCCGCAGGATGAGGAAGGT | CAACATCGAGCCTGGCAAACT | AGCGATAACGTTGTG | 15 |
| pyrBI | TATTGCATCAAATCTTGCGCCGCTT | CTGACGATGAGTATAAT | GCCGGACAATTTGCC | 146 |
| purF | TGGTTCGAATGGGATTGCCATCGCG | GTACTGTTTATCGCTACCCT | GATCGTTGGTGCTAT | 147 |
| glyA | TCCTTTGTCAAGACCTGTTATCGCA | CAATGATTCGGTTATACT | GTTCGCCGTTGTCCA | 148 |
| glyA region | ACACCAAAGAACCATTTACATTGCA | GGGCTATTTTTTATAAGAT | GCATTTGAGATACAT | 148 |
| argEp1 | TTACGGCTGGTGGGTTTTATTACGC | TCAACGTTAGTGTATTTT | TATTCATAAATACTG | 34 |
| argEp2 | CCCGCATCATTGCTTTGCGCTGAAA | CAGTCAAAGCGGTTATGTT | CATATGCGGATGGCG | 34 |
| argF | ATTGTGAAATGGGGTTGCAAATGAA | TAATTACACATATAAAGT | GAATTTTAATTCAAT | 149,150 |
| argI | TTTATGCTTTAGACTTGCAAATGAA | TAATCATCCATATAAATT | GAATTTTAATTCATT | 149 |
| aroG | AGTGTAAAACCCCGTTTACACATTC | TGACGGAAGATATAGATT | GGAAGTATTGCATTC | 151 |
| ilvB | CTTTGCTGAAAAATTTTCCATTGTC | TCCCCTGTAAAGCTGTGCT | TGTATAAATATTGTT | 152 |
| asnA | ATGCGGATTGATGATTCATTCTATT | TTAGCCTTCTTTTTTTAAT | GAATCAAAAGTGAGT | 153 |
| ompA | TATGCCTGACGGAGTTCACACTTGT | AAGTTTTCAACTACGTT | GTAGACTTTACATCG | 154-156 |
| ompB | TTTCGCCGAATAAATTGTATACTTA | AGCTGCTGTTTAATAT | GCTTTGTAACAATTT | 157 |
| argT | ACATCAGGACAATATTGCAACGTTT | TATTAACAAATTTAACGT | CGAATCGTTTTGCTG | 48 |
| crp | AAGCGAGACACCAGGAGACACAAAG | CGAAAGCTATGCTAAAAC | AGTCAGGATGCTACA | 158 |
| unc | TGGCTACTTATTGTTTGAAATCACG | GGGGCGCACCGTATAAT | TTGACCGCTTTTTGA | 159 |
| gnd | GCATGGATAAGCTATTTATACTTTA | ATAAGTACTTTGTATACT | TATTTGCGAACATTC | 160 |
| dnaA P1 | ATGCGGCGTAAATCGTGCCCGCCTC | GCGGCAGGATCGTTTACACT | TAGCGAGTTCTGGAA | 161 |
| dnaA P2 | TCTGTGAGAAACAGAAGATCTCTTG | CGCAGTTTAGGCTATGAT | CCGCGGTGCCCGATC | 161 |
| origin B | TTTCCACAGGTAGATCCCAAC | GCGTTCACAGCGTACAAT | ACGCCACTCTTAATA | 49 |
| origin E | TCAAGCCGACAAAGTTGAGTAGAAT | CCACGGCCCGGGCTTCAAT | CCATTTTCATAACGC | 49 |
| glyT | AAAGAGAGCTTCTCTCGATATTCAG | TGCAGAATGAAAATCAGGT | AGCCGAGTTCCAGGA | 56 |
| hisS | TGGCTCCCGAAACATTGAGGGAAGCGTTGAGGGTTCATTTTTATATT | | CAGAAAGAGAATAAA | 162 |
| rpsT P1 | TTATCGCGGAAAAGCTGTATTCACA | CCCCGCAAGCTGGTAGAAT | CCTGCGCCATCACTA | 163 |
| rpsT P2 | TTTGCACAAATCCATTGACAAAAGA | AGGCTAAAAGGGCATATT | CCTCGGCCTTTGAAT | 163 |
| rpsA | CACCACCTTAAGCATTGAGCAAGTG | ATTGAAAAAGCGCTACAAT | ACGCGCGCAGAAATT | 164 |
| rpmB-rpmG | TGTCTGTTCGGGACTTGAGCACATC | GCTGAGTCAGCGTATACT | ACGCACCTTTGAGAA | 165 |
| rpmH P1 | ATCCAGGACGATCCTTGCGCTTTAC | CCATCAGCCCGTATAAT | CCTCCAC | 161 |
| Ll1 | CGGCGATTTAATCGTTGCACAAGGC | GTGAGATTGGAATACAAT | TTCGCGCCTTTTGTT | 72 |
| T7 B | TTTATGATTATCACTTTACTTATGA | GGGAGTAATGTATATGCT | TACTATCGGTCTACT | 77 |
| T5 25 | CATAAAAAATTTATTTGCTTTCAGG | AAAATTTTTCTGTATAAT | AGATTCATAAATTTG | 166 |
| T5 26 | CTTAAAAATTTCAGTTGCTTAATCC | TACAATTCTTGATATAAT | ATTCTCATAGTTTGA | 166 |
| T5 28 | AGTTAAAATTGTAGTTGCTAAATGC | TTAAATACTTGCTATAAT | ATTTATATAAATTGA | 166 |
| T5 207 | TTTAAAAAATTCATTTGCTAAACGC | TTCAAATTCTCGTATAAT | ATACTTCATAAATTG | 166 |
| T4 57 | TGCTTTAGATTATCTTGATAAATTT | AACTCAGGTTATGATTATTAT | ATCGTTCCTGATACC | 167 |
| T4 45 | TTTAACGTTAATTGCTT | TATTAAATTAGTTATAAA | ATTAAATCTCATTTG | 168 |
| fd I | AATTCTCCCGTCTAATGCGCTTCCC | TGTTTTTATGTTATTCT | CTCTGTAAAGGCTGC | 108-110 |
| fd I' | GGCAAATTAGGCTCTGGAAAGACGC | TCGTTAGCGTTGGTAAGAT | TCAGGATAATTGTAG | 108-110 |
| fd II | ACAAAACATTAACGTTTACAATTTA | AATATTTGCTTATACAAT | CATCCTGTTTTTGGG | 108-110 |
| fd II' | TTTGAATCTTTGCCTACTCATTACT | CCGGCATTGCATTTAAAAT | ATATGAGGGTTCTAA | 108-110 |
| fd III | TTAAGAAATTCACCTCGAAAGCAAG | CTGATAAACCGATACAAT | TAAAGGCTCCTTTTG | 108-110 |
| fd IV | TGATAAATTCACTATTGACTCTTCT | CAGCGTCTTAATCTAAGCT | ATCGCTATGTTTTCA | 108-110 |
| fd IV' | TAAAATTAATAACGTTCGCGCAAAGGATTTAATAAGGGTTGTAGAAT | | TGTTTGTTAAATCTA | 108-110 |
| fd V | TTATTAACGTAGATTTTTCCTCCCA | ACGTCCTGACTGGTATAAT | GAGCCAGTTCTTAAA | 108-110 |
| fd VI | CGCTGGTAAACCATATGAATTTTCT | ATTGATTGTGACAAAAT | AAACTTATTCCGTGG | 108-110 |
| G4 A | GCTCCAAATAATGCTTGACTAATAC | TCAATCACCACTCTAATAT | GCCTCCCATCAAACG | 169 |
| G4 B | GGCAAATAAATAGCTTGCAAAACAC | GTGGCCTTATGGTTACTCT | ATGCCCATCGCAGTC | 169 |
| G4 D | TAAACAATCAATGCTTGACATACTG | AAAGAACGTGGCCTATTAT | CCACATCGTCAACTG | 169 |
| Mu Pe | TACCAAAAAGCAGCTTTACATTAAG | CTTTTCAGTAATTATCTT | TTTAGTAAGCTAGCT | 170 |
| pMB9 | AATACGCTCAGATGATGAACATCAG | TAGGGAAAATGCTTATGGT | GTATTAGCTAAAGCA | 171 |
| cloacin | TCATATATTGACACCTGAAAACTGG | AGGAGTAAGGTAATAAT | CATACTGTGTATATA | 172 |
| traT | GATATCGGTGGTAATTCATATGGTT | ATAGTTCAAAACGATATGAT | GAGTGAATCTTAATT | 173 |
| Tn3 tnpA | TGGACACTCAAACGAAGCCGTTTTA | CTATGTCTGATAATTTATAAT | ATTTCGAACGGTTGC | 174 |
| Tn3 tnpR | CGGCTTCGTTTGAGTGTCCATTAAA | TCGTCATTTTGGCATAAT | AGACACATCGTGTCT | 174 |

Figure 2. DNA sequences of proposed promoters. The sense strand sequences of possible promoters are aligned to maximize homology to the conserved -35 and -10 region hexamers. References for the sequence and the evidence that indicates that the sequence contains a promoter are listed. For the reasons discussed in the text, the current genetic and biochemical information does not allow precise location of the promoters within the sequences.

transcription experiments, and protection experiments (108,110). Conversely, it is also possible that some of the promoters in Figure 1 that were defined biochemically *in vitro* do not function *in vivo*. Thus, the defining characteristics employed here were intended to limit the uncertainty in the alignment of promoters for determination of a consensus sequence, but are not viewed as the sole criteria of promoter function.

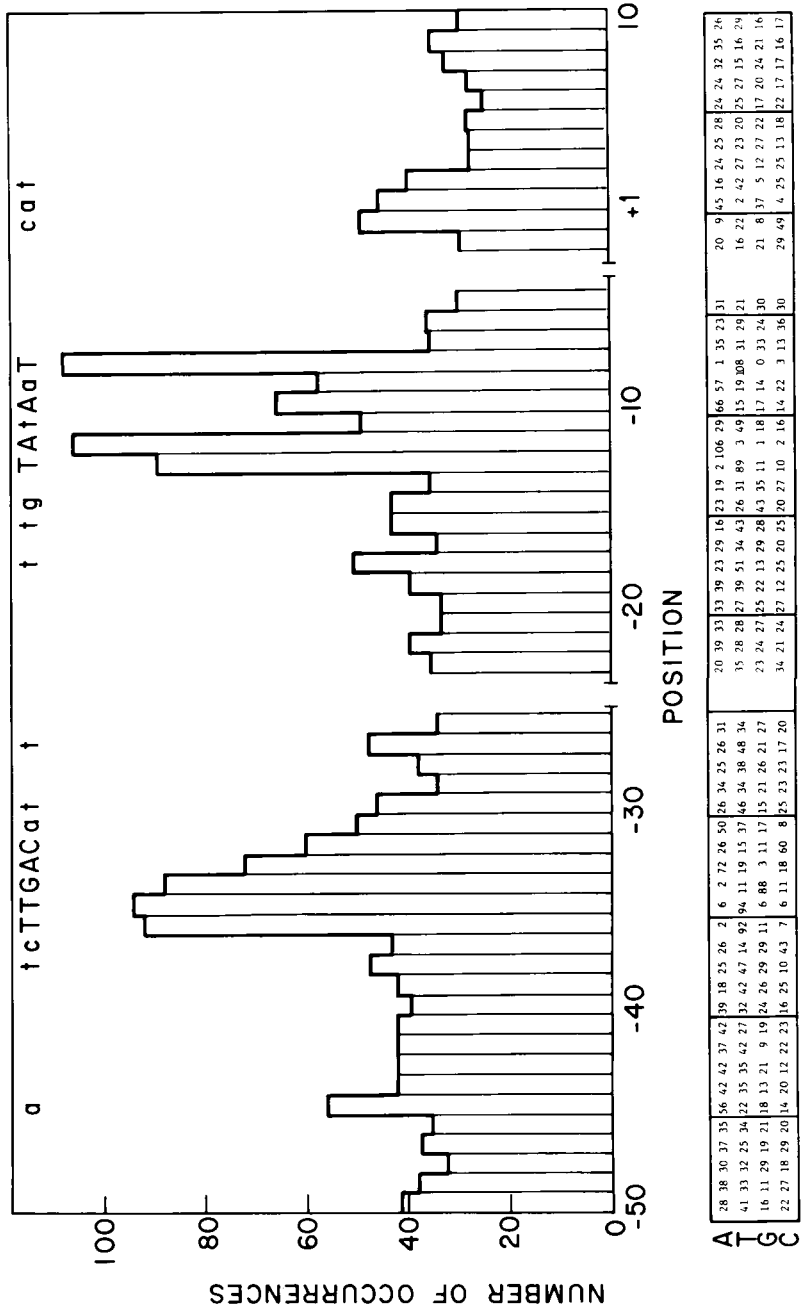
The alignment of the promoters in Figure 1 was based on several considerations. First, we tried to maximize homology to the 12 base pairs determined to be the most highly conserved among promoters previously compiled (205, 206). These bases were TTGACA around -35 and TATAAT around -10, with an allowed spacing of 15 to 21 base pairs between the two conserved sequences. When two alignments resulted in equal matches within the two hexamers, we assumed that a spacing of 17 base pairs was preferred. The optimum spacing and allowed range were selected on the basis of studies of promoters mutated by deletion or insertion between the -10 and -35 regions. Table 1 lists examples of spacer mutations. In all cases, the promoter was stronger if the spacing was closer to 17 base pairs. However, promoters with spacings of 15 and 20 base pairs were reported to retain partial function. All but 12 of the 112 promoters in Figure 1 could be aligned to maximize the homologies with spacings of 17 $\pm$ 1 base pairs.

In order to align promoters with different spacings, we placed two

Table 1
Mutations that change the spacing between the -35 and -10 regions.

| Promoter | Mutation | New Spacing | Phenotype | Reference |
|---|---|---|---|---|
| ampC | +1 | 17 | 15 X ↑ | 45 |
| $lacP^S$ | -1 | 17 | 10 X ↑ | 207 |
| $lacP^S$ | -2 | 16 | ≃ w.t. | 207 |
| P22 ant | -1 | 16 | weak ↓ | 100 |
| tyrT | -1 | 15 | 50 X ↓ | 191 |
| $lacP^+$ | +2 | 20 | 10 X ↓ | 208 |

Promoters in which insertion (+) or deletion (-) mutations have been characterized are shown. All of the phenotypes correspond to estimates of the changes in levels of expression *in vivo*, except for the $lacP^S$ mutations, which were characterized *in vitro*.


a tcTTGACat t t tg TAtAaT cat
NUMBER OF OCCURRENCES
POSITION
100
80
60
40
20
0
-50
-40
-30
-20
-10
+1
10
A
T
G
C

breaks in the sequences. The break between the -10 region and the transcription startsite was arbitrarily placed three base pairs downstream of the conserved -10 region hexamer. We chose the position of the break between the -10 and -35 regions by comparing the sequences of six pairs of analogous E. coli and S. typhimurium promoters. Most of the sequence differences between these highly homologous promoters occurred approximately 8 to 15 base pairs upstream of the -10 region hexamer.

The distribution of specific bases at each position is displayed in Figure 3. We have numbered the positions relative to the startsite of a "standard" promoter with spacings of 7 and 17 base pairs between the startsite and the -10 region, and the -10 and -35 regions, respectively. For purposes of discussing conserved base pairs, we have used Poisson statistics to express standard deviations from the expected random (1/4) occurrence of a base pair. We have arbitrarily chosen to define a consensus sequence consisting of strongly conserved and weakly conserved base pairs, present at frequencies greater than the expected by 6 and 3 standard deviations, respectively. These are indicated in Figure 3 by upper and lower case letters above the histogram.

Within the -35 region, the TTGAC sequence is strongly conserved. The A at -31 occurs at approximately the same frequency as four other weakly conserved bases within the -35 region: a T at position -38, a C at -37, a T at -30 and a T at -27. When the base at position -31 is not an A, a T is present at significantly greater than random frequency. Upstream of the -35 region is an 8 to 10 base pair A-T-rich region, with a conserved A at position -45.

Figure 3. The distribution of bases at each position in the promoter. The histogram displays the number of occurrences of the most prevalent base in the sense stand at each position. The number of occurrences of each base is tabulated below each column of the histogram. The positions have been numbered according to a promoter with the most frequent spacing between the regions of homology (see text). The bases that occur in at least 39% of the promoters (three standard deviations above expected random occurrence) are listed above the histogram. Bases that are greater than 54% conserved (6 standard deviations) are capitalized. Standard deviations are based on Poisson statistics. In this compilation, equal occurrence of the four bases at each site corresponds to 28 $\pm$ 5.3. From position -2 to +10 only 88 sequences are tabulated. These correspond to promoters for which the 5' end of the RNA has been determined. In this region equal occurrence corresponds to 22 $\pm$ 4.7.

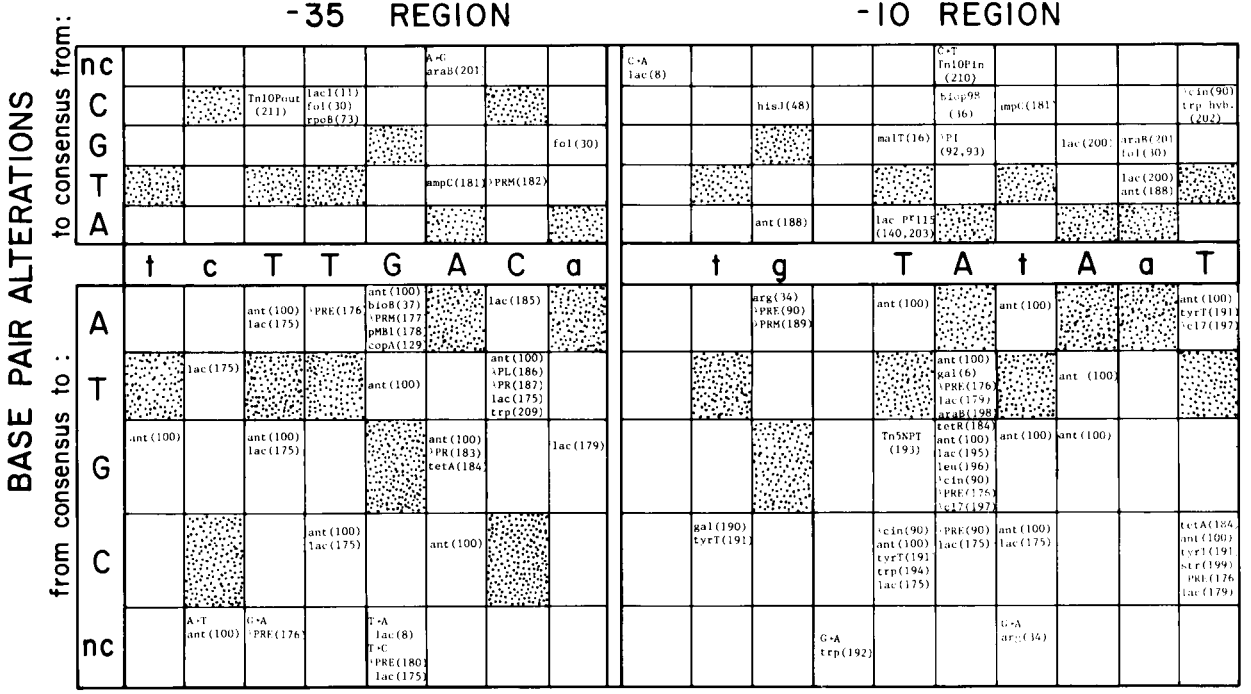



Figure 4. Location of promoter mutations. The base pair changes responsible for increasing or decreasing the initiation frequencies of promoters are shown. The consensus promoter is shown in the center of the grid. The mutations listed above this sequence are up-mutations that convert the indicated base to the consensus base. The mutations listed below are down-mutations that change the consensus base to the indicated base. Almost all of the mutations can be placed within this grid. The exceptions are the nonconsensus to nonconsensus changes (in the rows indicated "nc").

Four of the six base pairs in the -10 region hexamer are strongly conserved. The other two base pairs are weakly conserved, as are the T at -18, the T at -16, and the G at -15. The so-called "invariant T," while apparently not absolutely required for promoter function, is present in all but four of the wild-type promoters in this compilation. The A at -12 is present nearly as often; only six of the promoters do not share this homology.

Of the 112 promoters in Figure 1, only those 88 for which the 5' end of the transcript has been precisely determined were used to examine the sequence homologies around the startsite of transcription. A preference for a C at position -1 and a T at +2 was observed. No significant homologies were found downstream of +2. The spacing between the -10 region and the startsite is usually 6 or 7 base pairs, but varies between 4 and 8 nucleotides. The presence of multiple starts for some promoters indicates that the RNA polymerase is somewhat flexible in the selection of a startsite. Initiation with a purine is highly preferred. For most promoters, transcription begins with an A if one occurs within the required region, or a G if an A is not present. However, this generalization is far too simplistic because the availability of an A or a purine does not always preclude initiation with a G or a pyrimidine, respectively.

## PROMOTER MUTATIONS

The location of promoter mutations strongly suggests that the most highly conserved base pairs in the promoter are the main sequence determinants of promoter strength. About 75% of all sequenced mutations occur at the positions of the strongly conserved bases in the -10 and -35 regions of the promoter (Figure 4). Nearly all of the rest are located in positions of weakly conserved base pairs. In addition, all but seven of the mutations that decrease initiation frequency also decrease the homology of the promoter to the consensus sequence, while up-mutations increase the homology in all but three cases. This generalization is most strikingly illustrated by promoters for the phage P22 antirepressor and the *E. coli* lactose operon, for which many different single base pair mutations have been selected and sequenced. Only two of the mutations shown in Figure 4 occur at positions not included by our definition of consensus

sequence. The importance of some of the bases that are included (e.g., the A at -45 and the bases around the startsite) has not yet been demonstrated by genetic evidence.

The only up mutation that decreases homology to the consensus sequence is the A to G transition in the -35 region of araBAD. There are no down mutations that increase homology to the consensus sequence. However, seven of the mutations compiled in Figure 4 correspond to nonconsensus base pairs altered to other nonconsensus base pairs. These data suggest that a hierarchy of base pair preference could exist at some positions.

The demonstration that particular base pairs are highly preferred at some positions within the promoter and that mutations at these positions damage promoter function suggests that RNA polymerase specifically interacts with functional groups on these base pairs. It is also possible that certain bases at some positions interfere with promoter function. For example, at the following positions, one particular base is present at significantly lower frequency (by 3 standard deviations) than expected for random occurrence of three bases: a G at -42, a G at -33, and a C at -31. At most positions where strong homologies are observed, the other three bases all occur at such low frequency that a disfavored base cannot be assigned with certainty.

We draw two general conclusions from the literature survey presented here. First, the genetic and biochemical criteria we have used are the least ambiguous defining characteristics for promoters. Second, the location and sequences of most promoter mutations suggest that the consensus promoter sequence corresponds to maximal function. In the future, it may be possible to locate promoters by considering DNA sequence alone. Such attempts are currently speculative because the relative contribution of each base pair to promoter function cannot be assigned on the basis of homology information and mutant data alone. We expect that the current compilations will be useful for designing experiments that will better define promoter location and the determinants of promoter function.

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