MutS, MutL, and DNA helicase II are required for the mismatch- provoked excision step that occurs during *Escherichia coli* methyl-directed mismatch repair. In this study MutL is shown to enhance the unwinding activity of DNA helicase II more than 10-fold on a conventional helicase substrate in which a 35-residue oligonucleotide is annealed to a M13 circular single-stranded phage DNA under conditions where the two proteins are present at approximately molar stoichiometry with respect to the substrate. MutS- and MutL-dependent activation of DNA helicase II has also been demonstrated with a model substrate in which a 138-residue oligonucleotide was hybridized to a 138-nucleotide gap in an otherwise duplex 7,100-base pair circular DNA. Displacement of the oligonucleotide requires MutS, MutL, DNA helicase II, and ATP and is dependent on the presence of a mismatch within the hybrid region. Although DNA helicase II and Rep helicase share substantial sequence homology and features of mechanism, Rep helicase is inactive in this reaction.

*Escherichia coli* methyl-directed mismatch repair initiates via the mismatch-provoked incision of the unmethylated strand at a hemimethylated d(GATC) sequence in a reaction that involves the MutS- and MutL-dependent activation of the MutH d(GATC) endonuclease activity (1). The single-strand break thus produced may occur either 3' or 5' to the mismatch on the unmethylated strand and directs the exonuclease excision of that portion of the unmethylated strand spanning the incised d(GATC) sequence and the mispair (2, 3). Excision requires MutS, MutL, DNA helicase II, and an appropriate exonuclease. When the strand break that directs repair occurs 5' to the mismatch, excision requires RecJ exonuclease or exonuclease VII (3, 4), both of which support 5' → 3' hydrolysis (5, 6). For repair directed by a strand break 3' to the mismatch, the 3' → 5' hydrolytic activity of exonuclease I (7) is sufficient to meet the exonuclease requirement (2).

Since helicase II is required for excision from either side of the mismatch and because each of these exonucleases is specific for single-stranded DNA (5–7), the action of helicase II presumably serves to unwind the incised strand so as to render it exonuclease sensitive. According to this interpretation, the exonuclease functions in excision are secondary to those of DNA helicase II. We have therefore sought partial reactions in which MutS, MutL, and a mismatch might enhance the activity of helicase II. We show here that MutL stimulates helicase II activity on a conventional substrate and that helicase activity on incised duplex DNA is enhanced by MutS and MutL in a mismatch-dependent manner. The accompanying paper (8) demonstrates that MutS, MutL, and mismatch-dependent entry of helicase II into an incised heteroduplex occurs at the strand break with helicase entry biased so that translocation occurs toward the mispair.

**Experimental Procedures**

Proteins, DNA, and Nucleotides—MutS (9) and DNA helicase II (10) were purified as described. Rep helicase (11) was kindly provided by Timothy Lohman (Washington University, St. Louis, MO). λ Exonuclease was from Life Technologies, Inc., restriction enzymes and VENT polymerase from New England BioLabs, and T4 polynucleotide kinase from Amersham Pharmacia Biotech. *E. coli* MutL was purified by a modification of the method described previously (12) after subcloning the *mutL* gene from pAL51 (13) into a plasmid expression vector that had been cleaved with *NdeI* and *BamHI* to yield L1-pET3a. Briefly, a 180-liter culture of *E. coli* BL21(DE3)pLyS5/L1-pET3a was grown at 37 °C in LB broth supplemented with thymine (4 μg/ml), thiamine (10 μg/ml), glucose (10 mg/ml), and 10 mM KPO₄, pH 7.4. The culture was induced at 30 °C by addition of isopropyl-1-thio-β-galactopyranoside (Amersham) to 0.4 mM. The culture was chilled to 10 °C 2.75 h after induction and harvested by centrifugation. Cell paste (780 g) was stored at −70 °C. MutL was purified from 175 g of cell paste as described (12), except that the Bio-Rex 70 column was increased in size to 20 cm × 30 cm, and the concentration step and the Sephadex G-150 column were eliminated. Fractions from the Bio-Rex 70 column were pooled and dialyzed against 0.05 mM KPO₄ (pH 7.4), 0.05 mM KCl, 0.1 mM EDTA, 0.5 mM diithiothreitol (DTT), 2 mM phenylmethylsulfonyl fluoride, and 0.01 M KPO₄. In small aliquots in liquid N₂, and stored at −70 °C. The concentration of the MutL preparation used in this work, which was about 98% pure as judged by Coomassie-stained sodium dodecyl sulfate gels, was determined by Bradford assay (14). MutL preparations isolated by the previous procedure contain low levels of a DNA-dependent ATPase (12), which immunological analysis has shown to be DNA helicase II (not shown). MutL isolated as described above also contains helicase II, but the trace levels of the activity present had no effect on the experiments described here. When cited in molternal units, protein concentrations are expressed as monomer equivalents assuming 100% activity.

Wild-type M13mp2 and C103 M13mp2 phages, which differ at nucleotide 103 (T → C) in the lacZa gene (15), were gifts from Thomas Kunkel (National Institute of Environmental Health Sciences, Research Triangle Park, NC). [γ-32P]ATP was purchased from New England Nuclear. Oligonucleotides were synthesized by Oligo Etc.

Conventional Helicase Assays—The 35-residue oligonucleotide dATCGTCGGTATTTAATTGTTTCCCTAGATCTT was 5'-end-labeled using T4 polynucleotide kinase and [γ-32P]ATP (3000 Ci/mmol). After phenol extraction, phenol-chloroform-isoamyl alcohol extraction, and chloroform-isoamyl alcohol extraction, the labeled oligonucleotide 32

**The abbreviations used are:** DTT, diithiothreitol; RF, replicative form; bp, base pair(s); PCR, polymerase chain reaction.
was ethanol precipitated, resuspended in 25 μl of 10 mM Tris-HCl, pH 7.6, 1 mM EDTA, and residual ATP was removed by filtration through a 1-ml Sephadex G-50 column (Amersham Pharmacia Biotech, 7.5-cm × 0.196-cm) equilibrated in 10 mM Tris-HCl (pH 7.6), 150 mM NaCl, 1 mM EDTA (TNE). A 10-fold molar excess of oligomer was hybridized to 1.75 pmol M13mp2 viral strand in 20 mM Tris-HCl, pH 7.6, 150 mM KCl, 100 mM NaCl, 1 mM DTT in a 175-μl reaction (16). Incubation was at 95 °C for 1 min, 65 °C for 3 min, followed by slow cooling to room temperature. Excess oligomer was removed by filtration through a 1-ml Sepharose-4B column (Amersham Pharmacia Biotech, 7.5-cm × 0.196-cm) equilibrated with TNE.

Conventional helicase reactions contained 40 mM Tris-HCl (pH 7.6), 4 mM MgCl₂, 1 mM DTT, 50 μg/ml bovine serum albumin, 2 mM ATP, and 250 fmol/ml of conventional helicase substrate. Proteins were diluted as necessary into 20 mM KPO₄ (pH 7.4), 50 mM KCl, 1 mM DTT, 0.1 mM EDTA, 0.1 mg/ml bovine serum albumin, and added in 0.1 reaction volume. After incubation at 37 °C as indicated, reactions were terminated by addition of one-third volume 50 mM EDTA, pH 8.0, 0.5% sodium dodecyl sulfate, 0.02% bromphenol blue, 0.02% isocyanol blue, 2 μg/ml proteinase K, 40% by volume glycerol. After incubation at 50 °C for 5 min, samples were loaded onto an 8% polyacrylamide gel containing 44.5 mM Tris, 44.5 mM boric acid (final pH 8.4), 25% by volume glycerol, and 1 mM EDTA and subjected to electrophoresis at 8 V/cm for 4 h. Radioactivity was quantitated by using a Molecular Dynamics PhosphorImager.

**Duplex Helicase Assays**—Wild type M13mp2 RF DNA (500 μg) was cleaved with FspI and EcoRI. Reactions were deproteinized as described above and the 7059- and 138-bp products were separated by filtration through a 30-ml Sephacryl 400 column (Amersham Pharmacia Biotech, 25-cm × 0.785-cm) equilibrated with TNE. A gapped circle was prepared by mixing a 10-fold molar excess of the wild-type M13mp2 viral strands with 100 μg purified 7059-bp fragment, followed by alkaline denaturation, neutralization, and annealing (17). The gapped product was separated from excess viral strands by hydroxylapatite chromatography (17), dialyzed against 10 mM Tris-HCl, 45.5 mM boric acid (final pH 8.4), 25% by volume glycerol, and 1 mM EDTA and subjected to electrophoresis at 8 V/cm for 4 h. Concentrated 10-fold by butanol extraction, and filtered through Sephadex G-50 (7-cm × 0.19-cm) as described above.

A 138-residue single-strand oligomer was prepared for hybridization to the gapped circular duplex by PCR amplification of a segment of M13mp2 wild type RF DNA or C103 M13mp2 RF DNA using 5'-d(CACTGGCCGTCGTTTTACAACGTC) and 5'-d(GGGAAGGGCGATCGG) as primers. Reactions (0.1 ml) contained 375-ng template DNA (wild-type or C103 M13mp2 RF DNA depending on whether no mismatch or a G-T mismatch was to be generated in the case substrate) were performed as described under “Experimental Procedures” and sampled as indicated. Upper panel, reactions contained 94 fmol of MutL and 52 fmol of DNA helicase II (●) or 52 fmol of DNA helicase II alone (○). Lower panel, reactions contained 94 fmol of MutL and 350 fmol of Rep helicase (●) or 350 fmol of Rep helicase alone (○). At the concentration used, MutL displayed no detectable helicase activity (not shown).

**RESULTS**

**MutL Stimulates DNA Helicase II**—During initial attempts to identify a partial reaction dependent on MutS, MutL, and DNA helicase II, we found that near homogeneous preparations of MutL markedly stimulated helicase activity on a conventional substrate constructed by hybridization of a 36-residue oligonucleotide to M13mp2 viral strand DNA (see “Experimental Procedures”). Under conditions where helicase II was prevalent at one monomer equivalent per mol of substrate (as molecules), the addition of two monomer equivalents of MutL enhanced the initial rate of oligonucleotide displacement 11-fold (Fig. 1, upper panel). MutS and/or the presence of a G-T mismatch within the hybrid region had no effect on the rate of oligonucleotide displacement in the presence or absence of MutL (not shown).

![Fig. 1. MutL stimulates the unwinding activities of DNA helicase II and Rep in conventional helicase assays.](image-url)
E. coli Rep helicase and DNA helicase II are about 40% homologous at the sequence level (19), the two proteins can form heterodimers (20), and the duplex unwinding activity of both is stimulated by a 3'-single-stranded DNA tail. Low levels of MutL also stimulated Rep unwinding about 5-fold, although higher concentrations of the Rep activity were required to support significant unwinding with the substrate used here (Fig. 1, lower panel).

MutS and MutL Enhance Helicase Unwinding at a Strand Break in a Mismatch-dependent Manner—The failure to observe MutS or mismatch effects with the conventional helicase substrate might be due to the presence of mismatches within the secondary structure assumed by the 7 kilobases of single-stranded DNA in the molecule. To circumvent this potential problem, we constructed a duplex helicase substrate similar to that described by Washburn and Kushner (21) by hybridizing a 138-residue oligonucleotide to M13mp2 circular duplex DNA that contained a 138-nucleotide gap (Fig. 2). The 138-residue oligonucleotide was produced by PCR amplification using two different templates so that duplex helicase substrates could be constructed with or without a G-T mismatch between the two strand breaks (see “Experimental Procedures”).

As shown in Fig. 3, neither MutS nor MutL detectably altered the integrity of either homoduplex or G-T heteroduplex DNAs prepared in this manner. Furthermore, both DNAs supported only trace levels of unwinding by helicase II in the presence or absence of MutL or MutS. However, extensive displacement of the 138-residue oligonucleotide of the G-T heteroduplex occurred when all three proteins were present. The MutS, MutL, and helicase II-dependent unwinding reaction required ATP and Mg"+ and was not further enhanced by the addition of single-stranded DNA binding protein (not shown). It is noteworthy that the DNA and protein concentrations used in this experiment are those that have been determined to be optimal for the reconstituted mismatch repair reaction (2). Significant unwinding of the homoduplex control also occurred in the presence of MutS, MutL, and helicase II, but the degree of oligonucleotide displacement was considerably less than that observed with the G-T heteroduplex (Fig. 3). The kinetics of oligonucleotide displacement with these two substrates is illustrated in Fig. 4.

In view of the number of DNA manipulations involved in construction of the duplex helicase substrates, the background activity observed with the homoduplex control molecules might reflect polymerase errors occurring during the PCR amplification step used to prepare the 138-residue oligonucleotide (22–25) or damage incurred during denaturation and annealing steps. Given the random nature of production of such lesions, this hypothesis predicts that significant differences in mismatch dependence would be observed between independent sets of heteroduplex/homoduplex constructs. As summarized in Table I, this was in fact the case. With seven independent sets of heteroduplex/homoduplex constructs, the rate of unwinding of the G-T substrate ranged from 2.4 to 8.3 times that observed with the A-T substrate.
with the AT control with a mean value of 4.4. Nevertheless, other explanations for the homoduplex background cannot be excluded. For example, it is possible that the MutS and MutL pair might simply activate helicase II with duplex substrates. However, as shown in the accompanying paper, we have failed to observe detectable MutS, MutL, and helicase II-dependent unwinding of a similar circular homoduplex that contained a single nick and was prepared without using PCR methodology (8).

Activation of Unwinding by MutS and MutL Is Specific for DNA Helicase II—In contrast to mutU (uvrD) mutations that inactivate helicase II function in mismatch repair (17, 26), rep mutants are not mutators (27), and despite the significant MutL stimulation of Rep in conventional helicase assays (Fig. 1), the protein has no known function in mismatch repair. As shown in Fig. 5, activation of unwinding of the nicked duplex G-T substrate by MutS and MutL is specific for helicase II. Rep activity with this DNA was limited, and the presence of MutS and MutL had no significant effect on unwinding even at Rep concentrations 50 times that of the highest helicase II level tested.

**DISCUSSION**

Previous work has demonstrated that in addition to their roles in the initiation stage of methyl-directed repair, MutS and MutL are required for one or more subsequent steps (2), including the excision stage of the reaction (3). The experiments described here provide further support for involvement of these two proteins in the excision stage of the reaction. Results obtained with duplex substrates of the type shown in Fig. 2 indicate that the two proteins activate unwinding by helicase II in a mismatch-dependent manner. We have not directly addressed the mechanism of this effect, but it is possible that activation may involve several steps in the unwinding reaction.

The accompanying paper (8) demonstrates that mismatch-dependent unwinding by MutS- and MutL-activated helicase II initiates at a strand break. Whereas helicase II is capable of unwinding from a nick (28), this reaction requires very high helicase II concentrations with initiation being rate-limiting (29). Nevertheless, the finding that a genetically altered form of helicase II is selectively defective in unwinding from a nick suggests that this reaction may be biologically significant (30). In view of these findings, our observations with the duplex helicase II preparation indicate that MutS and MutL act in mismatch-dependent manner to enhance the rate of helicase II initiation at a strand break. As noted above, this effect is specific for helicase II and does not occur with 40% homologous Rep helicase, consistent with known requirements for helicase II in mismatch repair (17, 26).

In contrast to our failure to observe significant unwinding of a 138-residue oligonucleotide in the duplex substrate at low helicase II concentrations (Figs. 2–4), a 12-residue oligonucleotide in this type of molecule was previously shown to be efficiently displaced at low concentrations of the protein (21). We think it likely that these disparate results are due to the smaller size of the oligonucleotide in the latter substrate. Since helicase II binds at nicks (29), it is possible that proximity of the two strand breaks in the latter DNA results in a concerted effect on initiation of unwinding by the enzyme. Differences due to chain length effects may also reflect the relatively modest processive behavior of helicase II (31), and it has been shown that the number of base pairs unwound by the activity depends on the amount of the protein (32).

In addition to the MutS- and MutL-dependent activation of helicase II at a strand break, we have also found that MutL markedly enhances the activity of helicase II, and to a lesser extent the Rep enzyme, on conventional substrates. This effect is evident at very low protein concentrations (in the case of helicase II, about one monomer equivalent and 2 MutL monomer equivalents per 7-kb DNA molecule), indicating high specificity. In fact, preliminary experiments indicate that MutL and helicase II interact in the absence of RNA as judged by native electrophoretic analysis (33). Thus, in addition to its role with

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**TABLE I**

*Mismatch dependence of MutL, MutS, and helicase II-mediated oligonucleotide displacement from the duplex substrate*

Each entry represents an independent hetero/homoduplex preparation. Unwinding assays were performed at 30 °C for 10 min as described under "Experimental Procedures." The value shown for mismatch dependence corresponds to the activity ratio on the G-T heteroduplex versus the A-T homoduplex.

| Heteroduplex/Homoduplex preparation | Mismatch dependence |
|-------------------------------------|---------------------|
| 1                                   | 2.4                 |
| 2                                   | 3.3                 |
| 3                                   | 3.7                 |
| 4                                   | 3.9                 |
| 5                                   | 3.9                 |
| 6                                   | 5.0                 |
| 7                                   | 8.3                 |

Mean ± S.D.  
4.4 ± 1.8

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**FIG. 5.** Rep helicase does not substitute for DNA helicase II in the MutSL-dependent unwinding of the duplex substrate. The upper graph shows a titration of DNA helicase II in the presence or absence of both the MutS and MutL proteins. The reactions contained 23 fmol of G-T heteroduplex helicase substrate with the corresponding titration of DNA helicase II alone (●) or with 370 fmol of MutS and 250 fmol of MutL (■). The reaction conditions are described under "Experimental Procedures." The lower graph shows a similar titration with Rep helicase with the G-T substrate under the same conditions as above. Reactions contained 23 fmol of heteroduplex helicase substrate with the corresponding titration of Rep helicase alone (●) or in the presence of 370 fmol of MutS and 250 fmol of MutL (■). Incubation was at 30 °C for 10 min.
MutS and MutL Activation of Helicase II

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MutS in activating helicase II initiation at a nick, it is likely that MutL also functions as a helicase activator subsequent to initiation of unwinding. This activation could occur by increasing the processive behavior of the helicase by a direct interaction as is the case for dX174 gene-A protein and Rep helicase (34). The differential effects observed with the Rep helicase in the two assays are also consistent with the idea that MutS and/or MutL modulate helicase action at several levels of the unwinding reaction. MutL stimulation of both Rep and helicase II in conventional assays can be understood in terms of the 40% sequence homology shared by the two helicases (19). However, the failure of MutS and MutL to activate Rep unwinding at a single-strand break must be due to amino acid sequence elements that distinguish Rep from helicase II.

Although MutL is required for several steps in methyl-directed mismatch repair, precise molecular roles for the protein in the reaction have not been assigned. MutL binds to MutS-heteroduplex complexes (12), is required along with MutS and a mismatch for activation of the latent d(GATC) endonuclease of MutH (1), and stimulates the ATP-dependent MutS-catalyzed formation of heteroduplex DNA loops (35). Such observations have led to the suggestion that MutL serves to interface mismatch recognition by MutS to other components of the repair system (36, 37). The observations that MutL physically interacts with and activates helicase II are consistent with this view (33). Coupled with the finding that MutL is also required for the mismatch, MutS, and helicase II-dependent unwinding observed with nicked circular heteroduplex substrate, we think it likely that the protein has an important role in the mismatch-dependent loading of helicase II into the nicked heteroduplex, an event that is shown in the accompanying paper (8) to occur at the strand break.

A single hemimodified d(GATC) sequence is sufficient to provide strand specificity to heteroduplex repair by the E. coli methyl-directed pathway (4, 38), and mismatch-provoked incision of the unmethylated strand of this d(GATC) site by activated MutH (1) provides a strand break that is thought to serve as the initiation site for exonucleolytic removal of that portion of the new strand spanning the nick and the mispair (3). The latter conclusion is based on the finding that excision on a single d(GATC) site heteroduplex depends not only on MutS, MutL, and DNA helicase II (2, 3), but also requires an appropriate 3′ → 5′ or 5′ → 3′ single-strand exonuclease, depending on whether the MutH strand break is produced 3′ or 5′ to the mispair (4). By contrast, we have shown here that MutS, MutL, and helicase II are sufficient to displace a mismatched oligonucleotide from a heteroduplex in which a strand break is present on either side of the mismatch, raising questions concerning the biological significance of this exonuclease-independent reaction. Unfortunately, it is difficult to compare results obtained with the two types of heteroduplex. In the single d(GATC) site substrates examined previously, the distance between the MutH-produced strand break and the mispair is 1,000 bp (39), whereas nicks in the heteroduplex described here were located 45- and 92-bp to either side of the mismatch. Since activated helicase II can clearly unwind the latter substrate, concurrent exonucleolytic hydrolysis of the displaced strand product may be necessary for continued unwinding of the 1000 base pairs that separate the mismatch and the strand break in the former heteroduplexes. The distinct properties of these two types of substrates may be clarified by study of two d(GATC) site molecules and by examination of doubly incised heteroduplexes as a function of strand break-mismatch separation distance.

Note Added in Proof—Using two-hybrid analysis and protein affinity chromatography, Steve Matson and colleagues (Hail, M. C., Jordon, J. R., and Matson, S. W. (1998) EMBO J. 17, 1535–1541) have also demonstrated a physical interaction between MutL and DNA helicase II.

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REFERENCES
1. Au, K. G., Welah, K., and Modrich, P. (1992) J. Biol. Chem. 267, 12142–12148
2. Lahue, R. S., Au, K. G., and Modrich, P. (1989) Science 245, 160–164
3. Grilley, M., Griffith, J., and Modrich, P. (1993) J. Biol. Chem. 268, 11830–11837
4. Cooper, D. L., Lahue, R. S., and Modrich, P. (1993) J. Biol. Chem. 268, 11823–11829
5. Cohen, J. W., and Richardson, C. C. (1974) J. Biol. Chem. 249, 4553–4561
6. Lovett, S. T., and Kolodner, R. D. (1989) Proc. Natl. Acad. Sci. U. S. A. 86, 2627–2631
7. Lehman, I. R., and Nussbaum, A. L. (1964) J. Biol. Chem. 239, 2628–2636
8. Dao, V., and Modrich, P. (1998) J. Biol. Chem. 273, 9202–9207
9. Su, S.-S., and Modrich, P. (1986) Proc. Natl. Acad. Sci. U. S. A. 83, 5057–5061
10. Runyon, G. T., Wang, I., and Lohman, T. M. (1993) Biochemistry 32, 602–612
11. Lohman, T. M., Chao, K., Green, J. M., Sage, S., and Runyon, G. (1989) J. Biol. Chem. 264, 10139–10147
12. Grilley, M., Welsh, K. M., Su, S.-S., and Modrich, P. (1989) J. Biol. Chem. 264, 1900–1904
13. Lu, A.-L., Welah, K. Clark, S., Su, S.-S., and Modrich, P. (1984) Cold Spring Harbor Symp. Quant. Biol. 49, 589–596
14. Bradford, M. M. (1976) Anal. Biochem. 72, 248–254
15. Thomas, D. C., Roberts, J. D., and Kunkel, T. A. (1991) J. Biol. Chem. 266, 3744–3751
16. Matson, S. W. (1986) J. Biol. Chem. 261, 10169–10175
17. Lu, A.-L., Clark, S., and Modrich, P. (1985) Proc. Natl. Acad. Sci. U. S. A. 82, 4639–4643
18. Prolla, T. A., Pang, Q., Alani, E., Kolodner, R. D., and Liskay, R. M. (1994) Science 265, 1091–1093
19. Gilchrist, C. A., and Denhardt, D. T. (1987) Nucleic Acids Res. 15, 465–475
20. Wong, I., Amarantung, M., and Lohman, T. M. (1993) J. Biol. Chem. 268, 20386–20391
21. Washburn, B. K., and Kusnner, S. R. (1993) J. Bacteriol. 175, 341–350
22. Koshovang, P., and Thilly, W. G. (1989) Proc. Natl. Acad. Sci. U. S. A. 86, 9233–9237
23. Eckert, K. A., and Kunell, T. A. (1990) Nucleic Acids Res. 18, 3729–3744
24. Lundberg, K. S., Shomaker, D. D., Adams, M. W. W., Short, J. M., Sorge, J. A., and Mathur, E. J. (1991) Gene (Amst.) 108, 1–6
25. Cline, J., Braman, J. C., and Hogrefe, H. H. (1996) Nucleic Acids Res. 24, 3546–3551
26. Nevers, P., and Spatz, H. (1975) Mol. Gen. Genet. 139, 233–243
27. Matson, S. W., and Kaisser-Rogers, K. A. (1990) Annu. Rev. Biochem. 59, 329–349
28. Runyon, G. T., Bear, D. G., and Lohman, T. M. (1990) Proc. Natl. Acad. Sci. U. S. A. 87, 6383–6387
29. Runyon, G. T., and Lohman, T. M. (1993) Biochemistry 32, 4128–4138
30. Washburn, B., and Matson, S. W. (1997) J. Biol. Chem. 272, 552–557
31. Ali, J. A., and Lohman, T. M. (1997) Science 275, 377–380
32. Matson, S. W., and George, J. W. (1987) J. Biol. Chem. 262, 2060–2076
33. Yamaguchi, M. (1997) MutS, MutL, and DNA Helicase II Are Required for Mismatch-provoked Unwinding at a Strand Scission, Ph.D. thesis, Duke University
34. Arat, K.-I., Arai, N., Shlomai, J., Kohori, J., Polder, L., Low, R., Huber, U., Bertsch, L., and Kornberg, A. (1981) Proc. Natl. Acad. Sci. U. S. A. 84, 1482–1486
35. Matson, S. W., and George, J. W. (1987) Science 239, 1415–1420
36. Lahue, R. S., Su, S.-S., and Modrich, P. (1987) Proc. Natl. Acad. Sci. U. S. A. 84, 6829–6835