The eukaryotic DNA topoisomerase II is a dyadic enzyme that, upon ATP binding, transports one duplex DNA (T-segment) through a transient double-stranded break in another (G-segment). The path of the T-segment involves the sequential crossing of three gates along the dimer interface: the entrance or N-gate, the DNA gate, and the exit or C-gate. Coordination among these gates is critical for dimer stability and the prevention of chromosome damage. This study examines DNA transactions by yeast topoisomerase II derivatives defective in gate function. The results indicate that, although the N-gate is not required for G-segment cleavage, the DNA gate per se is not able to widen unless ATP binds to the N-gate. Next, a captured T-segment cannot be held in the interdomainal region between the N-gate and the DNA gate. Finally, the G-segment can be religated while a T-segment is held in the central cavity of the enzyme between the DNA gate and the C-gate. These quaternary couplings for gate opening and closing suggest that topoisomerase II ensures a transient DNA gating state, during which dimer interface contacts are maximized and backtracking of the transported DNA is minimized.

DNA transactions, mostly replication and recombination, naturally knot and entangle the chromosomes. If such tangles are not removed when daughter chromosomes are pulled into newly forming cells, they lead to DNA breaks and cell death. Type II topoisomerases contribute to this removal; they cleave newly forming cells, they lead to DNA breaks and cell death. If such a G-segment is in a circular DNA molecule, a high salt-resistant protein-DNA complex is formed (9, 14). The DNA gate corresponds to the DNA-protein platform constituted by the G-segment plus the active site for DNA cleavage and religation catalyzed by the B’ and A’ domains (15). Opening of the DNA gate requires, first, a chemical step and then, second, a mechanical step. The cleavage of both strands of the G-segment can be tightly coordinated during DNA cleavage and transport. This study examines DNA transactions by three derivatives of the yeast Saccharomyces cerevisiae topoisomerase II defective in gate function. As depicted in Fig. 1A, an N-terminal truncated topoisomerase II served as an N-gate-deleted enzyme. A top II mutant, in which the pair of active site tyrosyl residues had been replaced by phenylalanines, provided an enzyme that could not cleave DNA and open the DNA gate. A top II mutant, in which a pair of disulfide bonds form at the A’-A’ dimer interface, was used to prevent the opening of the C-gate. The results revealed several quaternary couplings among the three gates by which topoisomerase II may ensure stability of the dimer when the G-segment is cleaved and unidirectional transport of the T-segment.

EXPERIMENTAL PROCEDURES

Topoisomerases—All the derivatives of the S. cerevisiae DNA topoisomerase II are described elsewhere. Their plasmid constructs originated from YEpTOP2-PGAL1, a multicopy plasmid used in the overex-
polynucleotide kinase. For supercoiled removal assays, a single negatively supercoiled topoisomerase was prepared from a 2-kb pBR322 derivative. Supercoiled topoisomerases of the 2-kb plasmid were fractionated by agarose gel electrophoresis (21), and an individual topoisomer with a specific linking number difference of about −0.05 was recovered from the gel slice and purified by phenol extraction and ethanol precipitation. For decatenation assays, the dimeric DNA catenane KS6 (N5S), consisting of a 32P-labeled nicked circle singly linked to a supercoiled circle and containing distinct restriction sites in each, was constructed as follows. An EcoRI site of plasmid pKS5 (22) was converted into an XbaI site by linker insertion. The resulting plasmid, 7.2-kb pKS6, is a tandem dimer of two 3.6-kb sequences, differing in the presence of a single BamHI site in one half and a single XbaI site in the other half. Plasmid pKS6 was converted into a pair of 3.6-kb singly linked circles by Tn3 resolvase (22). Selective nicking of the circle containing the unique BamHI site was carried out by controlled digestion with BamHI in the presence of ethidium bromide (23). The singly nicked dimeric catenane was purified by density gradient centrifugation (24). Radiolabeling of the nicked circle with 32P was done by nick translation.

**Reactions, Filter Binding Assays, and Gel-blot Analysis**—Reaction Buffer A contained 50 mM Tris-HCl (pH 8), 150 mM KCl, 8 mM MgCl2, 7 mM 2-mercaptoethanol, and bovine serum albumin (100 µg/ml). Protein-mediated retention of DNA was carried out on Whatman GF/C glass fiber filters prepared and conducted as described previously (10, 25). Following DNA electrophoresis, the gels were blotted to nylon membranes. The blots were exposed (either directly or after hybridization with 32P-labeled DNA obtained by random priming) and quantified by phosphorimaging.

**RESULTS**

**Dimer Stability during DNA Cleavage by Topoisomerase II**

Lacking the N-gate Domain—Dimer stability of the N-gate-deleted top II bound to DNA was examined in vitro by a DNA transposition assay (Fig. 2). A radiolabeled 1.4-kb DNA fragment and an unlabeled 3.1-kb DNA fragment were mixed at
high concentration with stoichiometric amounts of either full-length or N-gate-deleted topo II. Following 8 h of incubation at 30 °C in the presence of 0 or 1 mM ATP, the reactions were quenched, and DNA fragments were examined by electrophoresis (Fig. 2, left). Cleaved products of both DNA fragments were seen in the reaction containing full-length topo II (Fig. 2, left, lane 2) and increased in the reaction with ATP (lane 3). Cleaved products of both DNA fragments were also seen in the mixture containing the N-gate-deleted topo II (Fig. 2, left, lane 4), although cleavage was not affected by ATP (lane 5). When the gel was transferred to a membrane and the radiogram was obtained (Fig. 2, right), only the labeled 1.4-kb fragment and its cleaved products were visible. Larger DNA molecules were not discernible in any reaction. Therefore, although the equilibrium level of DNA cleavage was comparable for the full-length and the N-gate-deleted topo II, DNA transposition (between labeled and unlabeled fragments), caused by the exchange of dimer halves linked to cleaved DNA, did not occur.

The N-gate Domain Is Required for Gating the Cleaved G-segment—If, in addition to cleaving DNA, the N-gate-deleted topo II opened the DNA gate, passive transport of another DNA segment could eventually occur. This possibility was examined with DNA substrates in which DNA transport is energetically favorable and easy to detect (26). The N-gate-deleted topo II was assayed for the single linking number change of a supercoiled circle (Fig. 3A) and for one-step decatenation of a dimeric catenane (Fig. 3B).

A single linking number topoisomer of a 2-kb plasmid was mixed with full-length or N-gate-deleted topo II at molar ratios of enzyme per DNA of -1. The reactions were supplemented with either ADPNP or ATP and incubated at 30 °C for 8 h. Two-dimensional gel electrophoresis was used to discern linking number changes in the input DNA (Fig. 3A, lane 1). In the reactions containing full-length topo II (Fig. 3A, lanes 2–4), the linking number was altered only when ADPNP or ATP was added. With ADPNP (Fig. 3A, lane 3), single DNA transport events catalyzed in the direction of supercoil removal changed the linking number of most of the topoisomer by +2 or +4 units. With ATP (Fig. 3A, lane 4), enzyme turnover generated a distribution of topoisomers with linking number values differing in units of 2 near the relaxed state. However, the linking number did not change in any of the reactions containing the N-gate-deleted topo II (Fig. 3A, lanes 5–7) or in the reaction containing full-length topo II without nucleotide (lane 2).

The dimeric DNA catenane KS6 (N:S), consisting of a radio-labeled nicked circle singly linked to a supercoiled circle, was mixed with the full-length or the N-gate-deleted topo II at molar ratios of enzyme per catenane of -1. The mixtures were incubated for 8 h at 30 °C in the absence or presence of ADPNP or ATP. The reaction products were analyzed by gel electrophoresis. The gel position of the catenane was marked by the labeled nicked circle (Fig. 3B, lane 1). The nicked circle was released from the catenane by cutting the supercoiled circle with endonuclease XbaI (Fig. 3B, lane 2). In the reaction containing full-length topo II plus ADPNP (lane 4), single DNA transport events resulted in the unlinking of ~60% of the catenane. In reactions containing full-length topo II plus ATP (Fig. 3B, lane 5), enzyme turnover resulted in the complete unlinking of the catenane. In contrast, in the reaction lacking nucleotide (lane 3) and the reactions containing the N-gate-deleted topo II (lanes 6–8), the circles were not at all unlinked. This and the above experiment demonstrate that although the N-gate-deleted topo II can cleave a G-segment, passive transport of another segment is unlikely to occur.

Capture of the T-segment Is Coupled to Cleavage of the G-segment—The DNA gate mutant topo II (YF) cannot cleave DNA and open the DNA gate. In the experiment depicted in Fig. 4, it was examined whether the YF mutant could trigger the closure of the N-gate and capture a T-segment. The dimeric DNA catenane KS6 (N:S), was mixed with the full-length or with the YF topo II at molar ratios of enzyme per catenane of -0.5. Mixtures were supplemented with ADPNP at 1 mM and...
incubated for 10 min at 30 °C. Each reaction volume was then split into two halves. Endonuclease XbaI, which linearizes the supercoiled circle of the catenane, was added to one half. After 20 min of incubation at 30 °C, NaCl at 1 M was added to all the reactions. The mixtures were then passed through glass fiber filters to retain high salt-resistant protein-DNA complexes. The protein-free DNA recovered from the filtrates and the protein-bound DNA recovered from the filters were examined by gel electrophoresis (Fig. 4).

In reactions with no topoisomerase added (Fig. 4, lanes 1–4), the dimeric catenane was found in the filtrate (lane 1). Freed nicked circles also appeared in the filtrate when the supercoiled circle of the catenane was linearized by XbaI (Fig. 4, lane 3). In reactions with full-length topo II (Fig. 4, wt, lanes 5–8), the nicked circle was unlinked from over 60% of the catenanes that reacted with topo II, and it was recovered in the filtrate (Fig. 4, lane 5). When the supercoiled ring was linearized, the nicked circle appeared mostly in the filtrate (Fig. 4, lane 7). These outcomes agreed with previous studies (10, 11). The topoisomerase was bound to a G-segment in the supercoiled circle and, upon binding ADP-νP, captured a T-segment located in the nicked circle with high probability. The T-segment was then transported and expelled through the C-gate. As a result, the unlinked nicked circle was found free in solution, whereas the supercoiled circle remained clamped by the topoisomerase.

In the reactions with the DNA gate mutant (Fig. 4, YF, lanes 9–12), no unlinked circles were found in the filtrate (lane 9) or in the filter (lane 10). However, the YF mutant had closed the N-gate around one or both rings of the catenane because nearly 50% of it was retained in the filter (Fig. 4, lane 10). When the supercoiled circle was linearized, all of the nicked circle appeared in the filtrate (lane 11). No freed nicked circle was retained in the filter held by the topoisomerase (Fig. 4, lane 12). Hence, the YF mutant had closed the N-gate, but it did not capture the expected T-segment located in the nicked circle. This outcome indicated that a conformation in which a captured T-segment is entrapped between the closed N-gate and DNA gate domains is unstable or unfeasible.

The G-segment Can Be Religated before the T-segment Exits the Topoisomerase through the C-gate—Because a captured T-segment cannot be held between the N-gate and the DNA gate, it must readily move through the DNA gate toward the central cavity of the enzyme. In the experiments depicted in Fig. 5, it was examined whether the T-segment could be held in the central cavity of the topoisomerase between the DNA gate and the C-gate. The C-gate mutant topo II, in which the C-gate can be locked by a pair of disulfide links, was used to prevent the exit of the T-segment. The religation state of the G-segment was then examined to determine whether the DNA gate remained open or had closed.

The DNA catenane KS6 (N:S) was mixed with the C-gate mutant at a molar ratio enzyme per catenane of ~0.5. The
mixtures were pre-incubated either in the presence of 2-mercaptoethanol to reduce disulfide bonds at the C-gate or in the absence of the sulfhydryl reagent to keep the C-gate cross-linked. ADPNP was then added to promote single-step DNA decatenation. After 10 min of incubation at 30 °C, NaCl at 1 M was added, and the reactions were passed through glass fiber filters to retain DNA circles trapped inside the topoisomerase. Protein-free DNA recovered from the filtrates and protein-bound DNA recovered from the filters were examined by gel electrophoresis (Fig. 5A). In the absence of the enzyme (Fig. 5A, lanes 1 and 2), the catenane was recovered in the filtrate (lane 1). In the presence of the enzyme (Fig. 5A, lanes 3–6), decatenation took place, and the same amount of nicked circle was unlinked in the reactions with and without 2-mercaptoethanol. Yet, in the reaction containing the reducing agent (Fig. 5A, lanes 3 and 4), the unlinked circles were found in the filtrate (lane 3). Conversely, in the reaction without reducing agent (Fig. 5A, lanes 5 and 6), the unlinked circles were retained by the enzyme in the filter (Fig. 5A, lane 6) because the T-segment could not exit through the C-gate.

To determine whether the G-segment was religated while the T-segment was inside the topoisomerase, a decatenation reaction in the absence of 2-mercaptoethanol was conducted as above. The molar ratio enzyme per catenane was ~1, and after the addition of ADPNP and 10 min of incubation, the reaction was split into three equal parts. Endonuclease XbaI, which linearizes the supercoiled circle of the catenane, was added to one part. Endonuclease BamHI, which linearizes the nicked circle of the catenane, was added to another part. No endonuclease was added to the third part. Following 30 min of incubation at 30 °C, NaCl was added to a final concentration of 1 M, and the three mixtures were passed through a glass fiber filter. Protein-free DNA and protein-bound DNA were analyzed by gel electrophoresis (Fig. 5B). In the reaction not treated with endonucleases (Fig. 5B, lanes 1 and 2), the topoisomerase interacted with nearly 70% of the catenanes and, upon ADPNP binding, carried out decatenation with 60% probability. As before, the unlinked nicked circles were retained in the filter (Fig. 5B, lane 2), because they were held inside the topoisomerase with the C-gate locked. Remarkably, the supercoiled circles, which provided a G-segment for decatenation, were found fully religated in the filter fraction (Fig. 5B, lane 2). When the nicked circles were linearized with BamHI (lanes 3 and 4), all of them appeared in the filtrate (Fig. 5B, lane 3). Therefore, the entrapped T-segments had slid away from the central hole of the enzyme. When the supercoiled circles were linearized with XbaI (lanes 5 and 6), all of them also appeared in the filtrate (Fig. 5B, lane 6). Hence, the G-segments gated during decatenation had also slid away from the closed topoisomerase. Consequently, the G-segment must have been religated while the T-segment was in the central hole of the enzyme.

**DISCUSSION**

The passage of the T-segment across the three gates of topoisomerase II implies that none of the dimer interfaces of the enzyme is permanent. Yet, the overall dimer must be firmly secured when the G-segment is cleaved and gated. Otherwise, dissociation or exchange of enzyme halves linked to cleaved DNA would cause chromosomal breaks or rearrangements. In this study, three different yeast topoisomerase II mutants were utilized to dissect quaternary couplings for gate opening and closing that control the DNA transport activity of the enzyme. It has long been known that DNA transport by topoisomerase II is ATP-dependent. ATP usage is mandatory even when topological interconversions of DNA are energetically favorable. For DNA transport to occur, the G-segment has to be cleaved (a chemical step) and then gated (a mechanical step). The B’ and A’ domains are sufficient to catalyze the cleavage step (15, 27) but likely are insufficient to carry out the gating step. Mechanical widening of the DNA gate platform, involving the B’ and A’ domains plus the cleaved G-segment, is probably impaired until ATP binds to the N-terminal domains. Prior to ATP binding, either the closed conformation of the DNA gate per se is highly stable or, alternatively, the N-terminal domains play some role in suppressing the opening of the DNA gate. The experiments with an N-gate-deleted enzyme support the first alternative.

The DNA transposition assay with an N-gate-deleted enzyme demonstrates the endurance of topo II against subunit exchange when DNA is cleaved. The equilibrium level of DNA cleavage achieved by the N-gate-deleted dimer is comparable with that of the full-length topo II (in the absence of ATP). However, the absence of transposition indicates that the N-gate-truncated dimer rarely falls apart while DNA is cleaved. Such stability can be attributed to the main A’-A’ dimer interface at the C-gate but also to a stable closure of the DNA gate. If the DNA gate were to open, passive transport of another DNA segment could then occur. The results show that passive transport of DNA is unlikely for the N-gate-deleted topo II. Although the G-segment can be cleaved, the DNA gate is either locked or does not open wide enough to permit the passage of another DNA segment. Therefore, binding of ATP to the N-terminal domains may not only serve up the capture of a T-segment (9) but may also unlock the DNA gate to open fully. This functional coupling could explain why DNA cleavage-rejoining equilibrium is found altered as long as the N-gate is kept closed by ADPNP after DNA transport is completed (28, 29).

Another functional dependence of the N-gate on the DNA gate is inferred from the YF mutant topo II, which cannot open the DNA gate. Upon nucleotide binding, this mutant closes the N-gate but does not capture a T-segment. The first implication of this result is that the closure of the N-gate does not require a transition state in which the G-segment has to be cleaved or gated. The second implication is that there is no space in which a captured duplex can be retained before the opening of the DNA gate. Structural studies have already indicated that a DNA double helix cannot be held in the dimer interface of the N-terminal domains. The crystal structure of the ADPNP-bound N-terminal domain of *S. cerevisiae* topo II shows that the channel in this dimer interface is ~6 Å wide, insufficient to confine a DNA duplex (13). Also, the archway formed by the dimerized N-terminal domain of *Escherichia coli* DNA gyrase is nearly 20 Å wide, but it has constrictions that would prevent the accommodation of duplex DNA (30). However, there are no structural data available on how the N-terminal domains are connected to the B’ domains in the DNA gate. Conceivably, the interdomainal region linking the N-gate and the DNA gate could be flexible enough to hold a captured duplex between the two gates. The present results preclude this last possibility. Consequently, the capture of a T-segment and the opening of the DNA gate must be mechanically coupled. Although ATP may be required for unlocking the DNA gate, the steric repulsion accompanying the entrapment of a T-segment by the N-gate may enforce the widening of the DNA gate.

After the T-segment passes through the DNA gate, it is promptly expelled through the C-gate (10, 11). Before exiting the enzyme, the T-segment must have passed through the central hole of the dimer. This cavity has positive surface charges, and, when the DNA gate opens, it is enlarged (15). Hence, full entry of the T-segment into this space should be favored. Alternatively, the T-segment may remain in the vicinity of the open DNA gate until the opening of the C-gate allows...
it to exit. The experiments with the topo II mutant, in which the C-gate can be locked with disulﬁde bonds, examined this issue. The results show, ﬁrst, that DNA transport probability is not affected and, second, that the DNA gate can close while a T-segment is trapped in the central hole of the dimer. These ﬁndings agree with that can be inferred from structural data. If the DNA gate and C-gate are closed, one DNA duplex could be accommodated, although tightly, in the central cavity of the enzyme (4, 31). The fact that the G-segment is found entirely religated corroborates that the open conformation of the DNA gate must be thermodynamically unstable. Therefore, the DNA gate likely opens only when a T-segment is trapped by the N-gate, and even then it may close quickly once the T-segment has passed.

As to the question of what opens the C-gate, it is clear that it allows only the escape of the T-segment. The G-segment never escapes through the C-gate even if it is dissociated by high salt from a topoisomerase II with the N-gate closed (9, 10). Because the closure of the DNA gate reduces the central cavity, steric hindrance could drive the exit of the T-segment through the C-gate. It was suggested that conformational changes at a pair of hinge structures at the A:A dimer interface would lead to a transient opening of the C-gate (32). The results with the C-gate-locked enzyme suggested that the transition state, which leads to the opening of the C-gate, could be reached following the entrapment of the T-segment in the central cavity and the relaxation of the G-segment. Yet, because these experiments did not provide temporal information for the opening of the C-gate, it could not be excluded that the T-segment exits the enzyme before the G-segment has been religated.

Fig. 6 summarizes a plausible pathway of conformational states for the three gates of topoisomerase II deduced from this study. One main inference is that quaternary couplings among the gates ensure the stability of the dimer during DNA cleavage. The various conformations of the enzyme-DNA complex seem to follow a "double lock" rule. Namely, a given gate cannot be open unless the other two are closed. Because the DNA gate and the C-gate may open only when they are triggered by the entrapment of a T-segment, transient opening of these gates would further maximize dimer interface contacts. The other main inference of this study is that quaternary couplings would enforce unidirectional transport of the T-segment along the dimer interface. Once the T-segment has reached the central cavity of the enzyme, backtracking of the T-segment is unlikely. If the DNA gate closes, reopening it by reverse transport of the T-segment could be energetically costly. Crystal studies indicate that widening of the DNA gate is coupled to a large rotation of the B’ domains (32). However, even if the DNA gate were reopened, there would be no space to accommodate the returned T-segment between the N-gate and DNA gate. Unidirectional movement of the T-segment may ensure its entrapment in the central cavity of the enzyme, which may be needed to trigger the opening of the C-gate.

The transport of one DNA double helix through the complete dimer interface of topoisomerase II stands as a fascinating molecular mechanism, which demands energetically well balanced conformational states during the critical DNA cleavage-religation steps. Backtracking of the T-segment would cause unnecessary breakages of the G-segment and no net DNA transport. Dissociation of the enzyme halves linked to cleaved DNA would cause chromosomal breaks and rearrangements. This study clarifies how topoisomerase II maximizes dimer interface contacts during DNA cleavage and minimizes back-tracking of the transported DNA. The conformational states inferred here may also provide new insights for rational design of chemotherapeutic agents targeting the DNA cleavage-religation equilibrium or the path of DNA along the dimer interface of topoisomerase II.

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REFERENCES
1. Champoux, J. J. (2001) Annu. Rev. Biochem. 70, 369–413
2. Wang, J. C. (2002) Nature Reviews MCB 3, 430–440
3. Wang, J. C. (1998) Q. Rev. Biophys. 31, 107–144
4. Berger, J. M. (1998) Curr. Opin. Struct. Biol. 8, 26–32
5. Lynn, R., Giaever, G., Swanberg, S. L., and Wang, J. C. (1986) Science 233, 647–649
6. Peng, H., and K. J. Marians (1993) J. Biol. Chem. 268, 24481–24490
7. Schultz, P., Olland, S., Oudet, P., and Hancock, R. (1996) Proc. Natl. Acad. Sci. U. S. A. 93, 5936–5940
8. Benedetti, P., Silvestri, A., Fiorni, P., and Wang, J. C. (1997) J. Biol. Chem. 272, 12122–12127
9. Roca, J., and Wang, J. C. (1992) Cell 71, 833–840
10. Roca, J., and Wang, J. C. (1994) Cell 77, 609–616
11. Roca, J., Berger, J. M., Harrison, S. H., and Wang, J. C. (1996) Proc. Natl. Acad. Sci. U. S. A., 93, 4057–4062
12. Olland, S., and Wang, J. C. (1999) J. Biol. Chem. 274, 21688–21694
13. Clasen, S., Olland, S., and Berger, J. M. (2000) Proc. Natl. Acad. Sci. U. S. A. 100, 10629–10634
14. Osheroff, N. (1986) J. Biol. Chem. 261, 9944–9950
15. Berger, J. M., Gamblin, S. J., Harrison, S. C., and Wang, J. C. (1996) Nature 379, 225–232
16. Tse, Y. C., Kirkegaard, K., and Wang, J. C. (1980) J. Biol. Chem. 255, 5560–5565
17. Rowe, T. C., Tewey, K. M., and Liu, L. F. (1984) J. Biol. Chem. 259, 9177–9181
18. Worland, S. T., and Wang, J. C. (1989) J. Biol. Chem. 264, 4412–4416
19. Curnen, P. R., Watt, P., and Wang, J. C. (1994) Mol. Cell. Biol. 14, 3197–3207
20. Morris, S. R., Harkins, T. T., Tennyson, R. B., and Lindsley, J. E. (1999) J. Biol. Chem. 274, 3446–3452
21. Keller, W. (1976) Proc. Natl. Acad. Sci. U. S. A. 72, 4876–4880
22. Krantzos, M. A., and Cozzarelli, N. R. (1983) Cell 32, 1513–1524
23. Barzilai, R. (1973) J. Mol. Biol. 74, 739–742
24. Radillo, R., Bauer, W., and Vinograd, J. (1967) Proc. Natl. Acad. Sci. U. S. A. 55, 1514–1521
25. Roca, J. (1999) Methods in Molecular Biology, DNA Topoisomerase Protocols (Osheroff N., and Bjornsti M. A., eds) pp 75–80, Humana Press, Totowa, NJ
26. Roca, J., and Wang, J. C. (1996) Genes Cells 1, 17–27
27. Reese, R. J., and Maxwell, A. (1980) J. Biol. Chem. 265, 19648–19653
28. Robinson, M. J., and Osheroff, N. (1991) Biochemistry 30, 1807–1813
29. Bjergbaek, L., Ringma, P., Nielsen, I. S., Wang, Y., Westergaard, O., Osheroff, N., and Andersen, A. H. (2000) J. Biol. Chem. 275, 13041–13048
30. Tingeay, A. P., and Maxwell A. (1996) Nucleic Acids Res. 24, 4868–4873
31. Pass, D., Bogden, C. E., and Berger, J. M. (1999) Nat. Struct. Biol. 6, 322–326
32. Morais Cabral, J. H., Jackson, A. P., Smith, C. V., Shikotra, N., Maxwell, A., and Liddington, R. C. (1997) Nature 388, 903–906

Fig. 6. Plausible pathway of conformational states of topoisomerase II-DNA complexes. The structural domains of topo II and the interacting G- and T-segments are pictured as in Fig. 1A. a, when the N-gate is open or deleted, the DNA gate and C-gate remain closed, and passive transport of DNA cannot occur. b, capture of the T-segment must be coupled to the opening of the DNA gate, because a duplex cannot be held between the closed N-gate and the DNA gate domains. c, when the T-segment reaches the central cavity of the enzyme, the DNA gate is able to close, and the G-segment can be religated. d, closure of the DNA gate and entrapment of the T-segment may trigger the opening of the C-gate. e, once the T-segment has escaped, the C-gate closes.
The Path of the DNA along the Dimer Interface of Topoisomerase II
Joaquin Roca

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