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60. To examine the possibility of sequence heterogeneity, we sequenced $(AC)_n$ and $(AT)_n$ alleles in a set of geographically diverse individuals. The $(AT)_n$ repeat consists of perfect, uninterrupted repeats in one European, three Africans, one Papua New Guinean, and one chimpanzee sequence (with alleles ranging from 135 to 139 bp). At the AC repeat, the 178-bp allele was sequenced in two Europeans and three Papua New Guineans and was found to be identical to the 178-bp allele published in GenBank. However, two 166-bp alleles sequenced in two African individuals (a South African Bantu-speaker and a Mende individual from Sierra Leone) had the sequence $(TA)_5(AA)_1(TA)_9(CA)_{10}$, which is 12 bp smaller than the 178-bp allele. This shorter allele was most likely the product of a single event, because geographically diverse Africans have identical sequences, suggesting that these A− alleles are identical by descent. Further sequencing analysis will be required to obtain a detailed understanding of the evolutionary history of the three microsatellite alleles. Sequencing conditions were as follows: for PCR products from individuals homozygous for microsatellite alleles, alleles from $(AC)_n$ were amplified with primers ACSEQF (5′-GAGACTGAGGTGGGAGGTTC-3′) and ACSEQR (5′-AAGGAAAAGTTCCTGGGTGG-3′), which produce a 235-bp product. Alleles from $(AT)_n$ were amplified with newly designed primers ATSEQF (5′-TGCATTTTATCACCCCCTTC-3′) and ATSEQR (5′-CAGCTAAGGTGGGCATAGTG-3′), which produce a 248-bp product. Amplification was performed with 50 to 100 ng of genomic DNA in a 25-μl (total volume) reaction mixture. The reaction mixture contained 10 pmol of each forward and reverse primer, 200 μM of each dNTP, 50 mM KCl, 10 mM tris-HCl, 1.5 mM $MgCl_2$, and 0.625 U of *Taq* polymerase. Samples were denatured for 1 min at 94°C, followed by 25 cycles of 94°C for 1 min, 60°C for 1 min, and 72°C for 1 min, followed by a 10-min extension at 72°C. The amplified products were purified with a Qiagen PCR purification kit and were cycle sequenced with a Beckman CEQ DTCS sequencing kit. Products were run and analyzed on a Beckman CEQ2000 automated DNA sequencer.
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REPORTS

Optical Control of Electrons During Electron Transfer

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The dynamics of electron transfer reactions in solution can be controlled with the use of a sequence of femtosecond laser pulses. In the charge transfer to solvent (CTTS) reaction of sodide (Na^-) in tetrahydrofuran, an initial light pulse launched the CTTS reaction, ejecting an electron into either an immediate or a solvent-separated Na^0:solvated electron contact pair. A second pulse was used to excite the electrons in the contact pairs, and a third pulse monitored the amount of Na^- produced through the back electron transfer. Excitation of the electrons in immediate contact pairs shut off the back electron transfer, whereas excitation of the electrons in solvent-separated pairs both enhanced and hindered the back electron transfer.

Examples of electron transfer (ET) reactions abound in biology, chemistry, and physics (*1*, *2*), but the large number of degrees of freedom in most ET systems makes it difficult to obtain a fundamental understanding of the charge transfer process. To build a complete microscopic understanding of ET reactions, it makes sense to study model systems that consist of atomic reactants. In this report, we show that femtosecond laser pulses can be used to control the motion of the electron as ET takes place in a model charge transfer system that has only electronic degrees of freedom, in this case, the transfer of a single electron from an atomic anion in solution to a nearby solvent cavity.

This reaction is an example of the well-known phenomenon of CTTS (*3*). Vertical excitation of a CTTS transition produces a localized excited state that is bound only by the polarization of the surrounding solvent. The resulting motions of the solvent molecules then cause the electron to be ejected from the excited parent anion, which produces a solvated neutral atom and a solvated electron (*4*). The photoinitiation of such reactions makes them amenable for study with ultrafast lasers because the entire photoexcited ensemble undergoes ET from the same temporal starting point (*5*–*8*).

In previous work, we have extensively characterized the CTTS transition of sodide (Na^-) in tetrahydrofuran (THF) (*5*–*7*). Alkali metal anions (as opposed to the more familiar cations) are formed in solution by the disproportionation of solid alkali metals (M) into the solvated ions M^+ and M^-. This reaction is usually catalyzed by cation complexing agents such as crown ethers (*9*). Our particular choice of Na^- is based on its spectroscopic convenience. The sodide CTTS absorption band is easily accessible in the visible (*10*), and the absorption spectra of the solvated electron (*11*) and sodium atom (*12*, *13*) products in THF are well known and spectrally well isolated (Fig. 1A). Because there are only electronic degrees of freedom, this system allows for detailed investigations of how the solvent affects the electronic energy of each species (*5*–*7*, *14*, *15*). Moreover, the lack of spectral congestion from vibrations and rotations allows for facile optical control over the dynamics of the back ET reaction.

Our previous femtosecond pump-probe experiments on the Na^-/THF system showed that excitation of the CTTS band produces a solvated electron (e_s^-) and a solvated sodium atom (Na^0) in 700 fs (*5*). The back ET reaction (recombination) to reform the parent sodium anion is not diffusion controlled (*6*) but can be explained by assuming that most of the ejected electrons remain in the immediate vicinity of their Na^0 partners in contact pairs. In some contact pairs, the electron resides in the same solvent cavity as the Na^0, which allows for direct nonadiabatic recombination within 1.5 ps; we refer to these species as "immediate" contact pairs. In other contact pairs, the electron and Na^0 products localize in adjacent solvent cavities and do not recombine for hundreds of picoseconds, depending on the solvent; we refer to these as "solvent-separated" contact pairs. The energy of the excitation pulse controls the branching ratio for formation of immediate and solvent-separated contact pairs (*6*). Our basic understanding of the kinetics of the CTTS process of Na^- is summarized in Fig. 1B (*7*).

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We show how ultrafast lasers can be used to manipulate the dynamics of ET in the Na^-/THF CTTS system. In particular, we show that excitation of the electrons in immediate contact pairs alters the recombination chemistry in a different way than excitation of the electrons in solvent-separated contact pairs, providing an avenue for optical control over the back ET reaction. The experiment makes use of three femtosecond laser pulses. The first pulse at 780 nm excites the Na^- CTTS transition and causes the electron to detach in 700 fs. The second pulse at 2000 nm excites the newly detached solvated electron. The third pulse at 490 nm measures the effects of the first two pulses by monitoring the number of sodium anions destroyed by the forward ET and regenerated by the back ET (Fig. 1A). The wavelength of the second pulse is chosen to excite the localized solvated electron into a highly delocalized electronic state that is more mobile than that of the ground state. We find that excitation of the electrons in immediate contact pairs moves them out of the solvent cavity with the Na^0, shutting off the rapid back ET. Excitation of the electrons in solvent-separated contact pairs, in contrast, can either assist or hinder recombination with Na^0.

Our results are closely related to work by Wasielewski and co-workers, who used femtosecond laser pulses to switch charge between two sites in an organic electron donor-acceptor complex (*16*). Also related are experiments recently performed by Barbara and co-workers, who altered the course of the diffusion-controlled reaction between hydrated electrons and various aqueous scavengers by exciting the hydrated electron (*17*, *18*). Our work extends these ideas by showing that optical excitation can be used to manipulate solvated electrons during the course of an ET reaction that starts from a donor-acceptor pair that is defined by the solvent. In particular, we can initially place the electron where we desire by choosing the appropriate CTTS excitation wavelength and then further manipulate its location, starting from either an immediate or solvent-separated contact pair, by carefully selecting the time at which the second excitation pulse is applied.

The solid curve in Fig. 2A displays the results of a standard two-pulse femtosecond pump-probe experiment on Na^- in THF. The CTTS band is excited at 780 nm, and the loss of absorption resulting from the removal of ground-state Na^- is probed at 490 nm. The data show the short-time (~1.5 ps) recovery of the Na^- absorption characteristic of the recombination of immediate contact pairs and a longer time (hundreds of picoseconds) recovery component due to the recombination of solvent-separated contact pairs (*6*, *7*). When the 2000-nm electron excitation pulse was applied either 0.9 ps (dot-dashed curve) or 1.5 ps (dashed curve) after the original 780-nm CTTS excitation pulse, the recombination dynamics changed markedly (Fig. 2A). For the 780-nm CTTS excitation wavelength we used, the great majority of the electrons (94%) were ejected into immediate contact pairs (*6*). Thus, for 780-nm excitation and the short time delays shown in Fig. 2, the electrons excited by the 2000-nm pulse are nearly exclusively in immediate contact pairs, and the effect of the 2000-nm electron excitation pulse is to shut down recombination. Because the electron's wave function in the immediate contact pair lies entirely within the same solvent cavity as its Na^0 partner, the delocalization of the wave function that occurs upon 2000-nm excitation serves to move electron density out of the immediate cavity, shutting off the back ET. An analysis of the data in Fig. 2A with our previously developed kinetic model (*5*, *7*) indicates that application of the 2000-nm pulse provides a greater than fourfold enhancement in the probability for the electron to escape recombination.

The change in the Na^- recovery kinetics resulting from the application of 2000-nm pulse (Fig. 2B, inset, the difference between the 780/2000/490 and 780/490 experiments in Fig. 2A) also provides information on the nature of the solvent motions that drive the back ET reaction. The difference signals are identical, indicating that the effect of the electron excitation pulse is independent of when it is applied (as long as it is applied at times early enough to excite predominantly the electrons in immediate contact pairs, as discussed further below). Moreover, the data in the inset to Fig. 2B show that it takes some time after application of the 2000-nm pulse to shut off the back ET reaction: The early-time portion of the difference signals fit well to a ~700-fs exponential rise, similar to what we observed for the forward ET after CTTS excitation (*5*). For the forward excitation, the rate of electron ejection is limited by the translational motions of the first-shell solvent

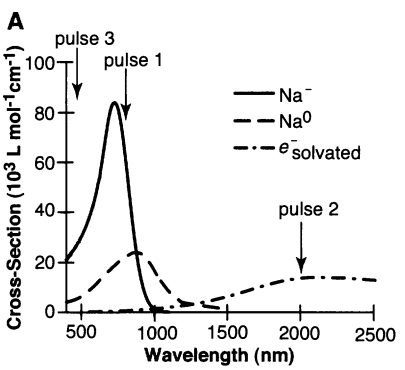

Fig. 1. (**A**) Steady-state absorption spectra of the major kinetic species in the CTTS reaction of sodide (Na^-) in THF: ground-state Na^- [solid curve (*5*, *10*)], the solvated neutral sodium atom [dashed curve (*12*, *13*)], and the solvated electron [dot-dashed curve (*11*)]. The arrows show the spectral positions of the femtosecond light pulses used in the experiments. (**B**) A simplified kinetic scheme for the CTTS transition of Na^- in THF based on (*5*–*7*); a more detailed scheme would also include the possibility of dissociation of the immediate and solvent-separated contact pairs. The branching ratio between immediate contact pairs, solvent-separated contact pairs, and free solvated sodium atoms-solvated electrons is determined by the wavelength of the CTTS excitation pulse.

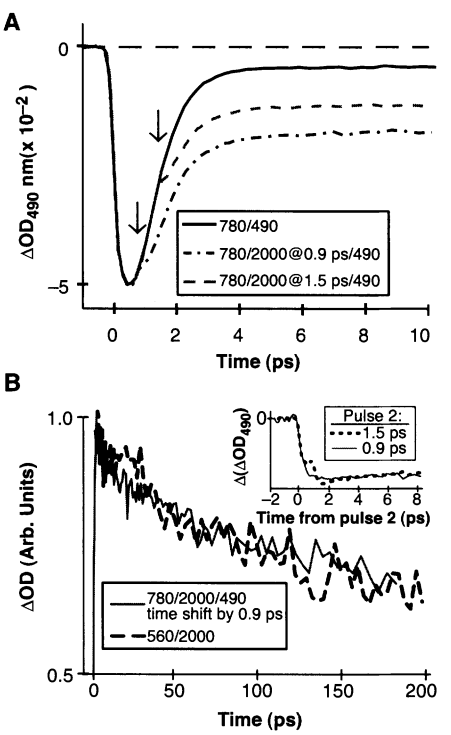

Fig. 2. (**A**) Comparison of a standard two-pulse experiment (780-nm pump, 490-nm probe; solid curve) with a three-pulse electron control experiment (780-nm pump, 2000-nm electron excitation, 490-nm probe) on Na^- in THF, with the electron excitation pulse arriving during the recombination of immediate contact pairs, either 0.9 ps (dot-dashed curve) or 1.5 ps (dashed curve) after the 780-nm pump pulse. The arrows indicate the arrival time of the 2000-nm electron excitation pulse. (**B**) Comparison of the three-pulse experiment [thin solid curve; same as dashed curve from (A) with the zero of time shifted to coincide with the 2000-nm reexcitation pulse] with a two-pulse experiment in which Na^- is excited near 560 nm and the recombination dynamics are probed at 2000 nm (dashed curve); the curves have been arbitrarily scaled for better comparison. (Inset) The short-time dynamics of the difference between the two- and three-pulse signals shown in (A) (thin solid curve for 0.9-ps delay, dotted curve for 1.5-ps delay); these two curves have been scaled to the same maximum for better comparison.

molecules that accommodate the change in cavity size as the electron is detached from the Na^- to form the contact pair (*7*). The appearance of this same time scale upon excitation of the e_s^- suggests that the same types of solvent translational motions are involved in shutting off the back ET. Reexcitation of the electron does not prevent recombination until after the solvent molecules have rearranged to allow the electron to escape the immediate solvent cavity.

What happens to the electrons excited by the 2000-nm pulse after they escape from the immediate contact pairs? Our previous work on the Na^- system argued that the energy of the CTTS excitation photon determines the relative fraction of electrons that are ejected into immediate and solvent-separated contact pairs or into the bulk (Fig. 1B) (*7*). If only the total energy applied is important, then the successive application of 780-nm (1.6 eV) and 2000-nm (0.6 eV) light pulses should produce the same solvent-separated contact pairs and bulk e_s^- as made by CTTS excitation with a single 560-nm (2.2 eV) pulse. The main part of Fig. 2B contrasts the kinetics after application of the 2000-nm pulse in the three-pulse experiment (solid curve) against the results of a two-pulse experiment in which the recombination dynamics are monitored after 560-nm excitation of the CTTS band (dashed curve). Within the noise, the two transients are identical. Hence, the effect of the 2000-nm pulse is to reexcite the e_s^- in immediate contact pairs and redistribute them into solvent-separated pairs and bulk e_s^-, providing an enhancement of the electron escape probability similar to that produced if the same total energy had been available in the initial CTTS excitation pulse.

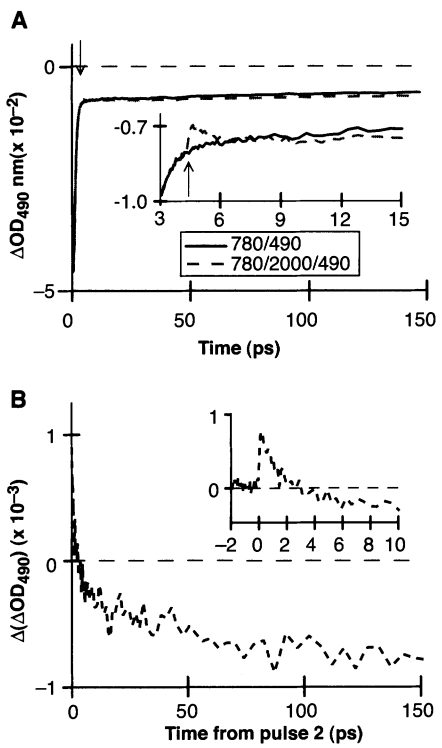

Fig. 3. (**A**) Comparison of a standard two-pulse experiment (780-nm pump, 490-nm probe, solid curve) with a three-pulse electron control experiment (780-nm pump, 2000-nm electron excitation, 490-nm probe, dashed curve) on Na^- in THF, with the electron excitation pulse arriving 4.4 ps after the 780-nm pump pulse so that recombination of immediate contact pairs is complete. (Inset) The same data near the arrival time of the 2000-nm electron excitation pulse on an expanded scale. The arrow marks the arrival time of the 2000-nm electron excitation pulse. (**B**) Dynamics induced by the 2000-nm excitation pulse [dashed curve; difference between the three- and two-pulse data shown in (A)]. (Inset) The same data on an expanded time scale.

Figure 3A compares the results of the two-pulse 780/490 experiment (solid curve) and the three-pulse 780/2000/490 experiment (dashed curve) when the 2000-nm electron excitation pulse is delayed to arrive 4.4 ps after the original CTTS excitation. At this time, all of the immediate contact pairs have recombined, so the 2000-nm pulse acts solely to excite the electrons in solvent-separated contact pairs. Immediately after applying the 2000-nm pulse, the back ET reaction is enhanced: More Na^- is formed after excitation of the electron than would be created naturally from the recombination of solvent-separated contact pairs, to produce a less negative absorption signal. At longer times, the electron excitation pulse is seen to suppress the back ET: Less Na^- is produced in the long run when the 2000-nm pulse is present, which leads to a more negative absorption signal. This dual behavior results from the expansion of the spatial wave function of the excited electrons upon 2000-nm excitation. The wave function of some of the reexcited electrons will have improved overlap with the adjacent solvent cavity containing the Na^0, leading to an immediate enhancement of recombination. The wave function of the remaining reexcited electrons, however, will have enhanced amplitude in regions of the solvent away from the Na^0. This leads to the destruction of solvent-separated contact pairs and shuts off some of the longer time (hundreds of picoseconds) recombination. The relative fraction of excited electrons that undergo recombination enhancement as opposed to suppression likely depends on the range of delocalization provided by the 2000-nm pulse (*17*) and the solid angle that the Na^0 cavity subtends from the electron's position in the solvent-separated contact pair. Overall, the effect of the 2000-nm pulse on some of the electrons in solvent-separated contact pairs is to accelerate recombination: The back ET occurs within 1 ps of reexcitation, rather than on the hundreds of picoseconds time scale typical of solvent-separated pairs. For the remainder of the electrons, however, the 2000-nm pulse disrupts the long-time recombination of solvent-separated pairs by delocalizing the electron further into the solvent, leading to a ~20% net enhancement of the electron escape yield.

Figure 3B shows how the back ET kinetics change when the 2000-nm pulse is applied to solvent-separated contact pairs (difference signal for the 780/2000/490 and 780/490 transients in Fig. 3A). The positive difference signal at early times, which reflects the enhanced production of Na^- due to the 2000-nm pulse, has a delayed appearance that fits well to a ~700-fs exponential rise. This rise time is consistent with a delay in recombination caused by the electron having to force the first shell solvent molecules around the Na^0 to translate outward to create space for the new Na^-. This time matches the forward CTTS ejection time because similar solvent motions are involved: The principle of microscopic reversibility requires that the same solvent motions should be responsible for both removal and reattachment of the electron from the atomic sodium core. The difference signal also shows decay dynamics on a ~2-ps time scale, which we tentatively assign as cooling of newly created sodium anions. In other words, the effect of the third pulse at early times is to create Na^- as soon as the solvent configuration becomes favorable enough for the electron to remain attached. The solvent surrounding the newly created Na^-, however, has not had time to reach equilibrium. As the surrounding solvent equilibrates and the local temperature rises, the absorption spectrum of the Na^- shifts to the red (*19*). This redshift of the absorption spectrum leads to a decrease of the Na^- absorption cross section at 490 nm, producing the observed decay of the difference signal on the ~2-ps time scale (*20*). Solvation dynamics that shift the spectra of photoexcited probe molecules on the ~2-ps time scale in THF have been observed in other experiments (*21*).

In addition to allowing control over the back ET, the three-pulse experiments also verify the existence of immediate and solvent-separated contact pairs after CTTS excitation of Na^- in THF. We had proposed the existence of the two different kinds of contact pairs on the basis of the observation of nondiffusive recombination kinetics after CTTS excitation (*6*, *7*). When the kinetics of recombination were probed throughout the ~2000-nm absorption band of the e_s^-, the dynamics were independent of probe wavelength. This result suggests that the spectrum of the e_s^- does not change with time: e_s^- that recombine at early times have the same spectrum as the electrons that recombine at longer times (*5*). Because the absorption spectrum of e_s^- in nonpolar fluids is likely the result of a tran-

sition from a localized solvent-bound ground state to the continuum of the solvent conduction band (*22*), the absorption of electrons in contact pairs should be similar to the absorption of the free e_s^-. Although the spectra are similar, the stark contrast between the difference signals for the three-pulse experiments shown in the insets of Figs. 2B and 3B verifies that indeed two different species are absorbing the 2000-nm pulse of light. Because recombination is initially promoted when the electron is excited at long times and hindered for excitation at short times, we argue that two different species account for e_s^- in the immediate and solvent-separated contact pairs.

The ET reaction being controlled in this case, the recombination of the CTTS electron with Na^0 to reform Na^-, starts from one of two well-defined configurations, an immediate or solvent-separated contact pair. Both configurations undergo a spontaneous ET reaction when the electron excitation pulse is applied to alter the reaction dynamics. When the electron excitation pulse arrives at early times, the excess energy delocalizes the electrons in the immediate contact pairs, distributing them out into the solvent in much the same manner as if a single excitation pulse had been used with the same total energy. The effect of the excitation pulse in shutting off the recombination of immediate contact pairs is rate-limited by the translational motions of the solvent required to eject the electron from the immediate cavity. If the electron excitation pulse comes at later times when no immediate contact pairs are present, the delocalized electron has some probability to transfer back onto the nearby Na^0 (once the solvent has rearranged), creating a hot Na^- that cools on the ~2-ps time scale. Some of the electrons in solvent-separated contact pairs that absorb the 2000-nm pulse can move in directions away from the sodium atom, resulting in a cessation of recombination at longer times.

All of these results demonstrate that it is possible to use femtosecond pulse sequences to control both the position of the electron and the rate of recombination in CTTS reactions. These CTTS systems have only electronic degrees of freedom, so we can control ET reactions without having to precisely shape the femtosecond pulses, as would be necessary to control the nuclear degrees of freedom in photodissociation reactions (*23*). For the Na^- CTTS reaction, the wavelength of the excitation pulse can be chosen to create a desired initial ratio of immediate to solvent-separated contact pairs. Subsequent excitation at 2000 nm can then be used to selectively break up the immediate pairs or to manipulate the recombination dynamics of solvent-separated pairs. The use of electron excitation pulses at different wavelengths or with different relative polarizations may offer an even finer degree of control, possibly allowing further enhancement of the recombination of solvent-separated pairs. Perhaps most importantly, the use of multiple femtosecond pulses provides a window on the solvent motions that drive ET reactions.

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20. It is also possible that the 2000-nm pulse promotes the electron into the excited CTTS state, Na^-*, and that this state absorbs 490-nm light. The 700-fs rise of the difference signal would then represent the time for internal conversion to form Na^- from Na^-*. In (*5*), we determined the spectrum of Na^-* and found no oscillator strength at 490 nm. However, we expect the position of the spectrum to be very sensitive to the local solvent configuration around the Na^-*, and the solvent configuration around Na^-* produced directly from the ground state is quite different from that produced by reexcitation of the electron in a contact pair. Further experiments with different probe wavelengths should clarify this issue.
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Impact of Polymer Tether Length on Multiple Ligand-Receptor Bond Formation

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The promoters of cell adhesion are ligands, which are often attached to flexible tethers that bind to surface receptors on adjacent cells. Using a combination of Monte Carlo simulations, diffusion reaction theory, and direct experiments (surface force measurements) of the biotin-streptavidin system, we have quantified polymer chain dynamics and the kinetics and spatial range of tethered ligand-receptor binding. The results show that the efficiency of strong binding does not depend solely on the molecular architecture or binding energy of the receptor-ligand pair, nor on the equilibrium configuration of the polymer tether, but rather on its "rare" extended conformations.

How is the molecular structure and range of interaction of a given tethered receptor-ligand pair related to the interaction range and time required for binding? Our ability to answer this question is crucial to our understanding of biorecognition and bioadhesion. To investigate the impact of tether length and dynamics in modulating receptor-ligand binding, we chose a poly(ethylene glycol) (PEG) tether and the well-characterized ligand-receptor pair streptavidin-biotin (*1–5*). In the experimental setup, shown schematically in Fig. 1, the biotin moiety is attached to the distal end of a flexible PEG tether while the streptavidin group is immobilized on the opposing membrane surface (*6*). Figure 2A shows the measured interaction forces between the two surfaces at varying separation distances for three tether lengths, expressed in terms of the polymerization index N (the number of CH_2CH_2O units) = 45, 75, and 142 (*7*).

The ligand-receptor binding range increases