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Anomalous Viscosity of a Racemate: a Simple Experiment Demonstrating Chirally Induced Spin Selectivity

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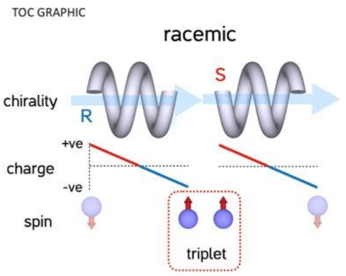

Abstract: **It has been known for over a century that racemic solutions of hydrogen-bonded compounds are less viscous than their component enantiomers, but this fact has so far remained unexplained. Here we confirm it using enantiomers of lactic acid, and compare it to molecular dynamics simulations of lactic acid viscosity. The effect is absent in classical MD. We suggest that the anomalous viscosity of racemates may be due to a recently discovered magnetic intermolecular force due to spin-dependent charge reorganization.**

Electrons flowing through chiral phases become spin polarised. This chirally-induced spin selectivity effect (CISS) was first seen in photoelectrons tunneling through polypeptides [1]and DNA[2], and later by a variety of methods in other systems[3,4] including living organisms[5]. The mechanism by which CISS occurs is still not fully understood[6,7]. Recently another type of CISS, called spin-dependent charge reorganization or SDCR, has been described in situations where no DC electron current flows[8], and spin selectivity acts instead on fluctuating electron currents moving within a polarizable molecule. We illustrate the SDCR mechanism in figure 1. In CISS, direct currents flow through chiral media from a source to a sink. In SDCR, by contrast, the currents are due to fluctuations in the electron density of the molecule, and flow transiently[9]. The key feature of SDCR is that fluctuations in nearby molecules are correlated as the transient dipoles interact. The correlation in the currents, combined with spin selectivity, causes a correlated spin redistribution in neighboring molecules. Depending on the chirality, this spin redistribution will either result in an attractive (singlet) or a repulsive (triplet) magnetic force between molecules. SDCR, if present, should therefore affect intermolecular forces between two adjacent molecules depending on whether they have the same or opposite chirality. Specifically, a novel magnetic force is predicted to exist, attractive between homochiral pairs and repulsive in heterochiral ones. This was confirmed by atomic force microscopy[10]. We speculated that this force might cause a measurable depression in the kinematic viscosity of a racemic mixture. There is to date no fully quantitative theory of liquid viscosity[11,12], but attractive intermolecular forces, especially hydrogen bonds, clearly play an important role. For example, 2-hydroxypropionic acid (lactic acid, figure 2) is at least fifty times more viscous than propionic acid. One would therefore expect viscosity to be steeply dependent on hydrogen bond strength. Here we report that racemic lactic acid is less viscous than its enantiomers. Classical molecular dynamics viscosity simulations of lactic acid enantiomers show no such viscosity difference, consistent with it being a quantum effect.

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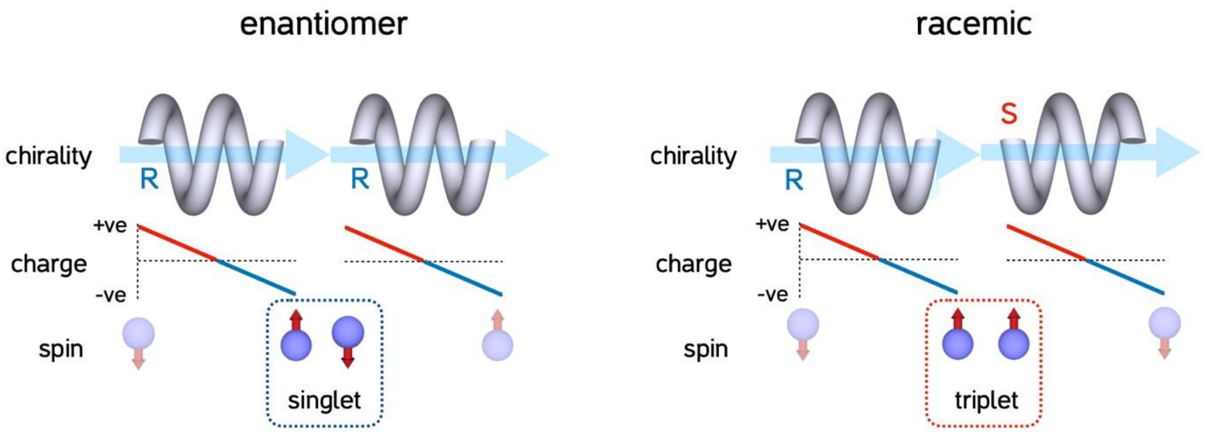

Figure 1: Origin of the magnetic force between chiral molecules. **Chirality**: Two polarizable chiral molecules, depicted as springs, undergo correlated fluctuations in their electron clouds (blue arrows). **Charge**: At the peak of one of these fluctuations, both molecules behave as charged dipoles aligned head-to-tail (tilted line). The correlated intramolecular electron currents that give rise to the transient dipole are subject to spin selectivity, and cause a partial excess of one spin orientation at one end of the molecule and a partial depletion at the other end. **Spin**: When the molecules are homochiral (enantiomer, left), the unpaired spins at the point of intermolecular contact are of opposite polarity (singlet), causing a small attractive magnetic force. With molecules of opposite chirality (racemic, right), spins of the same polarity face each other (triplet), and the force is repulsive. Reversing the direction of the intramolecular current inverts spin polarities but does not change the sign of the forces.

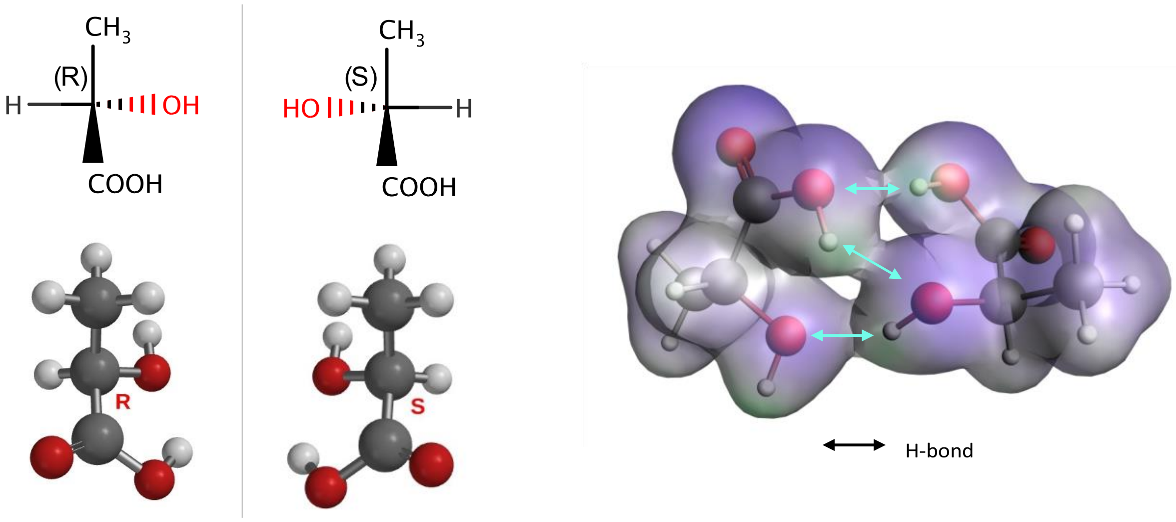

Figure 2. Left: enantiomers of lactic acid. **Right:** two S-lactic acid molecules connected by three hydrogen bonds (blue arrows) between hydroxyl groups. The electron density surfaces are fused at the locations of the hydrogen bonds. Blue color indicates regions of relative negative electrostatic potential. Conformation optimized with ML potential ANI-2X, DFT electron structure single point B3LYP-DZP.

Typical viscometry experiments using a bob-and-cup arrangement require sample volumes of 20 ml or more. For enantiomerically pure chemicals, this quantity is prohibitively expensive for at least one enantiomer. Unusually among commonly available chemicals, lactic acid (2-hydroxypropanoic acid) is available in quantity as either enantiomer with good chemical and enantiomeric purity. Pure lactic acid is solid, but 90% solutions in water are liquid. Viscosity falls steeply with dilution, and variability in water content causes small differences in the viscosity of commercial lactic acid solutions at the same nominal concentration. The lactic acid enantiomers used in these experiments had slightly different viscosities. We did not adjust them by dilution insofar as the effect of mixing was unambiguous.

For simplicity and low cost, we used a bob and cup rotary viscometer and controlled temperature by immersing the cup in a 5-liter water bath kept at room temperature (19-21C). Temperature variations were less than 0.2 C during the course of an experiment. Bob rotation speed was 6 rpm, and viscosity data was updated every 10 seconds during experimental runs lasting 1 hour. The results are shown in figure 3. Remarkably, in every run the viscosity of the 50-50 racemic mixture was lower by approximately 7% than the mean of the two enantiomers.

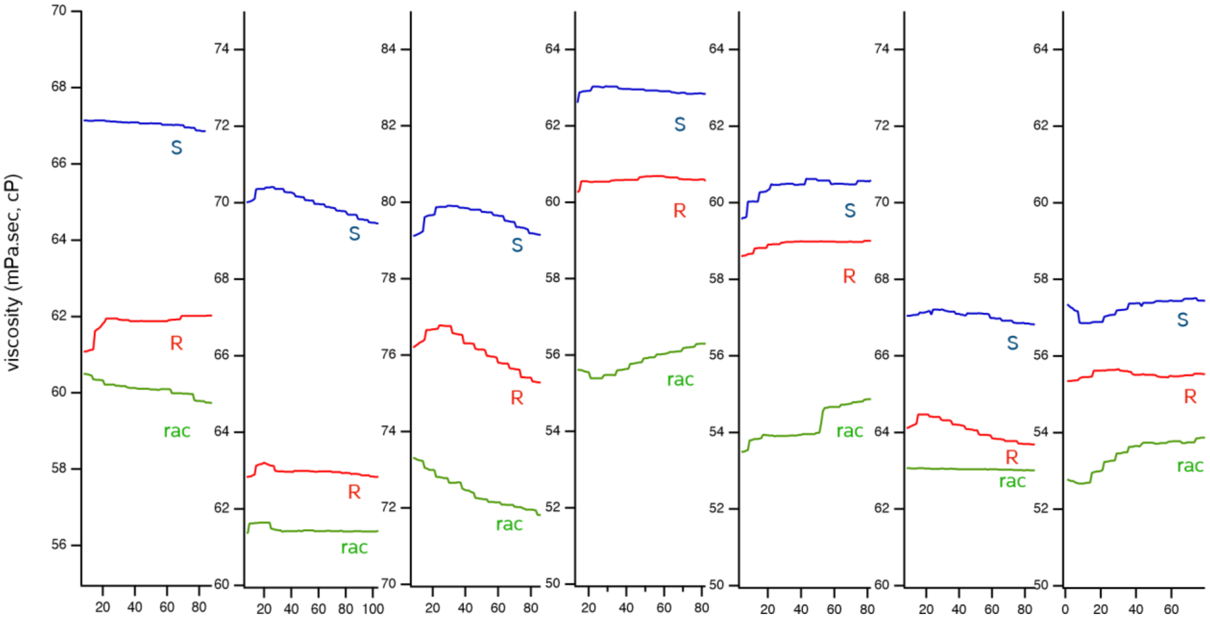

Figure 3. Viscosity measurements of lactic acid enantiomers and their 50:50 racemic mixture. Enantiomers were used without viscosity adjustments from the stock solutions. R is somewhat more viscous than S. The raw data from the viscometer recordings is shown. Each panel shows one series of measurements in which the viscosities of R, S, and the freshly mixed racemic mixture of lactic acid were measured. After an initial transient due in part to the viscometer performing a running average between successive measurements, the traces settle to values varying by ≈2% during the period of measurement. In all experiments, the viscosity of the racemic mixture lies below the viscosity of either enantiomer. Assuming that racemic viscosity, absent any other effects, should be midway between R and S viscosities, the viscosity deficit is approximately 5 mPa.s, or roughly 7%.

To rule out purely geometric factors potentially affecting viscosity, we performed molecular dynamics simulating a rotary viscometer. The bob is an alpha helix of 20 serines terminated at both ends with methyl groups. Serine was chosen to maximize hydrogen-bonded interactions between its side-chain hydroxyls and the solvent. The cup is a cubical box 7nm on the side, and the serine bob was placed in its center with its axis parallel to one face. To compare viscosities, we rotate the helix on its axis and monitor the resulting torque for both enantiomers of lactic acid and for the racemic mixture. Viscous flow dissipates mechanical energy to heat, and in the linear regime, total energy dissipated is the integral of torque x angle. The results are shown in figure 4.

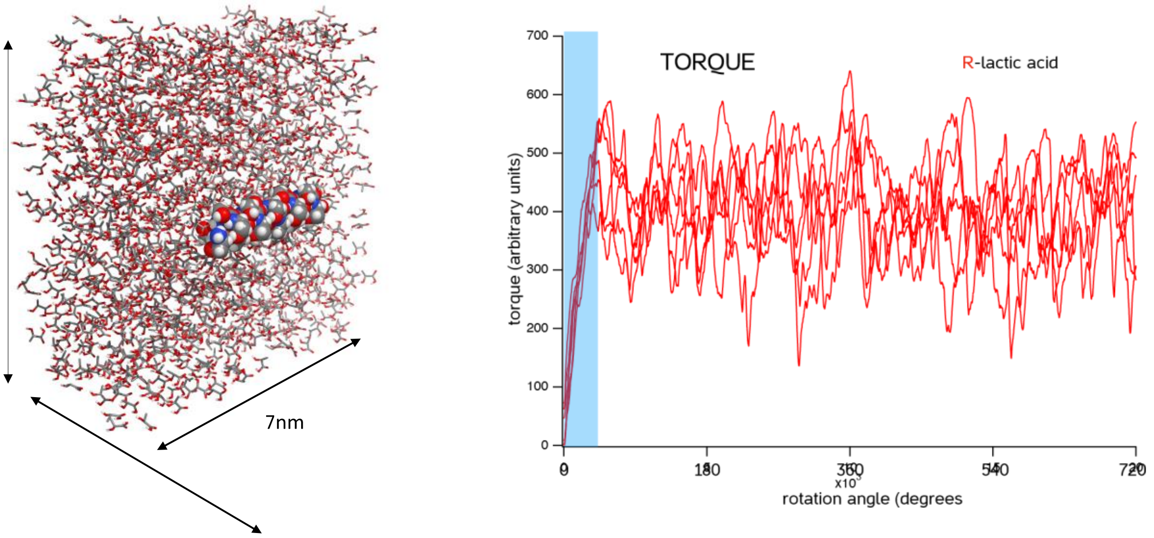

Figure 4A. Left: molecular dynamics setup. An alpha helix of 20 serines is positioned at the center of a cube 7 nm on the side, its axis parallel to the bottom face. The cube is filled with the appropriate enantiomer of lactic acid or the racemic mix. For clarity, only half the lactic acid molecules are shown. **Right:** The graph shows torque fluctuations in six separate MD runs of the serine helix in R-lactate solvent. Two regimes are visible. For the first 30 or so degrees (blue region), torque increases linearly with displacement, indicating elastic behavior. Thereafter, a viscous regime is established and rotation causes random changes in torque around a mean. integration of the torque curves yields work for each run.

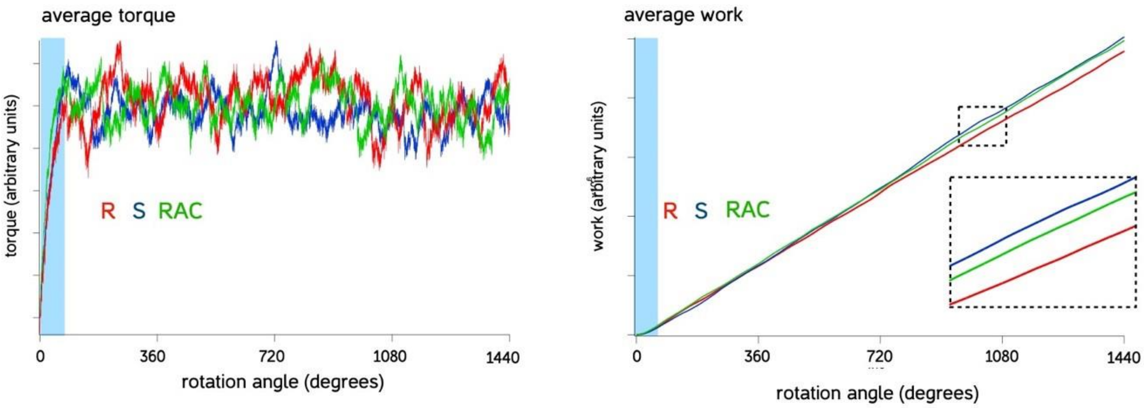

Figure 4B. Left: averaged torques for six “R” runs (red), 4 “S” runs (blue) and 5 racemic runs (purple). No systematic effect of the enantiomeric composition is visible. **Right:** integrated averages. The racemic curve lies midway between R and S. The inset shows the curves within the dotted box at higher magnification with the racemic line midway between the enantiomers.

The molecular dynamics simulations show no significant difference in the dissipation caused by helix rotation in either enantiomer of lactic acid as compared to their racemic mixture.

A literature search revealed that the anomalously low viscosity of racemic solutions of hydrogen-bonded liquids had in fact been known for well over a century, though apparently unmentioned in recent decades[13–16]. At the time the effect was attributed to hypothetical racemate complexes forming in the solution, but these were never found. Molecular dynamics simulations of racemic mixtures show no obvious anomaly[17]. Our simple experimental setup confirms the viscosity anomaly, while the MD simulations of viscosity of lactic acid are further evidence against the notion that some form of association between enantiomers could explain it.

What else could account for our results? **1-** The solutions of lactic acid we used were not pure, since some water must be present for lactic acid to be a liquid. The amounts of water in the two samples were slightly different, or their viscosities would have been identical. The water concentration in the racemic must therefore be midway between those of the two enantiomers, and there could conceivably exist a local viscosity minimum. There is, however, no evidence of any anomaly in the monotonic viscosity vs dilution curves of lactic acid[18]. **2-** The formation of a small amount of lactic acid polymers affecting the viscosity cannot be ruled out, but it is hard to see how mixing them could yield the observed effect. **3-** Differential effects of chirality on enantiomer drift in viscous flow are known[19–22], but none would lead to a low racemic viscosity even if some enantiomer separation occurred at the low shear values used in these experiments.

In conclusion, the most parsimonious explanation of the effect we observe is a decrease in intermolecular force similar to the one predicted by SDCR and seen in atomic force measurements [10]. It may be possible to detect a reduction in hydrogen bond strength in racemates directly by vibrational spectroscopy[23]. If its origin in SDCR is established, the anomalous viscosity of racemates would be a classroom demonstration of the first fluid-mechanical effect since superfluidity to require a quantum mechanical explanation.

Methods: 90% R and S lactic acid solutions were obtained from Musashino Chemical Laboratory Ltd, Tokyo. Viscosity measurements are made with a Baoshishan NDJ-5s Viscometer (Vevor UK) with a 25 ml bob-and-cup #0 rotor accessory. Data acquisition was via an RS-232 interface and wifi-enabled AirDrive Serial Logger Pro accessed via an iPhone. The cup was immersed in a 5 l water bath at room temperature for thermal inertia.

MD simulations were done with Gromacs[24], adopting the CHARMM27 force field for the helix. Compatible parameters for the lactic acid were obtained using SwissParam[25]. Lennard-Jones and electrostatic interactions were truncated at 1 nm. The timestep was 2 fs. Each system was equilibrated during 30 ps of MD in the NVT ensemble at room temperature[26], followed by 30 ps in the NPT ensemble at atmospheric pressure and room temperature[27]. During equilibration, the heavy atoms of the helix were harmonically restrained. Each production run consisted of 4 ns in the NPT ensemble. Helix rotation was achieved using the pivot-free isotropic potential method[28] with a spring constant of 50 kJ/(mol nm^2). The helix was rotated along its axis at a rate of 0.36 degree/ps and the torque required to do so was recorded every 0.2 ps.

Supporting information: Gromacs input file for the enforced rotation of the alpha helix of 20 serines on its axis.

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