

The violation of the Pauli limit seems to result from an intrinsic spin–orbit coupling effect, characteristic of a monolayer. This spin–orbit interaction results in an effective magnetic field: $\mathbf{H}_{\text{SO}}(\mathbf{k}) \propto \mathbf{k} \times \boldsymbol{\epsilon}$, where the mirror symmetry of the layers restricts the crystal field, $\boldsymbol{\epsilon}$, to the plane of the motion of the 2D-confined electrons with finite momentum \mathbf{k} . Whereas adjacent mirror-symmetric planes cancel out the spin–orbit field in bulk crystals, the absence of inversion symmetry in a single 2H transition metal dichalcogenide layer allows the manifestation of this interaction as a Zeeman-type out-of-plane spin polarization.

This effective Zeeman field has been computed to be of the order of several hundred tesla, which easily exceeds the limits of the world's largest magnet laboratories. It therefore strongly locks the spin of the electron to the out-of-plane orientation. It is worthwhile noting that the Zeeman field takes opposite directions in opposite corners of the hexagonal Brillouin zone. This favours the formation of Cooper pairs between electrons of opposite valleys with opposite spin polarizations — a phenomenon referred to as Ising pairing (Fig. 1). Most importantly, it prevents the alignment of the spin to in-plane

magnetic fields and hence protects the superconducting state.

Non-centrosymmetric systems have yielded interesting examples of extraordinarily robust superconductivity in heavy Fermion superconductors⁹, intermetallic alloys¹⁰ and hexagonal pnictides¹¹. However, this is the first time that the Pauli limit has been surpassed in a true crystalline 2D lattice. The findings break new ground for the application of transition metal dichalcogenides in the study of symmetry breaking in layered superconductors, where the presence of a spin–orbit interaction could lead to the realization of 2D topological superconductivity.

More than four decades since the discovery of superconductivity in the transition metal dichalcogenides and their intercalation compounds¹², these materials are back in the spotlight¹³. With a handful of intrinsically superconducting members in addition to the rest of the semiconducting compounds that can be gate-tuned into superconductors, this metal dichalcogenide family now provides a library of crystalline (unconventional) superconducting layers. The ease with which these materials can be processed, in addition to their crystalline nature and the high level

of perfection possible in van der Waals interfaces opens the door to the study of superconductivity in an exceptionally clean and versatile platform. They add up to the existing collection of insulating, semiconducting and metallic 2D crystals, unlocking superconductivity for its use in unprecedented heterostructures. □

Efren Navarro-Moratalla and Pablo Jarillo-Herrero are in the Department of Physics, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA.

e-mail: pjarillo@mit.edu

References

- Geim, A. K. & Novoselov, K. S. *et al. Nature Mater.* **6**, 183–191 (2007).
- Wang, Q. H., Kalantar-Zadeh, K., Kis, A., Coleman, J. N. & Strano, M. S. *Nature Nanotech.* **7**, 699–712 (2012).
- Frindt, R. F. *Phys. Rev. Lett.* **28**, 299–301 (1972).
- Ayari, A., Cobas, E., Ogundadegbe, O. & Fuhrer, M. S. *J. Appl. Phys.* **101**, 014507 (2007).
- Staley, N. E., Wu, J., Eklund, P. & Liu, Y. *Phys. Rev. B* **80**, 184505 (2009).
- Cao, Y. *et al. Nano Lett.* **15**, 4914–4921 (2015).
- Xi, X. *et al. Nature Phys.* **12**, 139–143 (2016).
- Saito, Y. *et al. Nature Phys.* **12**, 144–149 (2016).
- Settai, R., Takeuchi, T. & Onuki, Y. *J. Phys. Soc. Jap.* **76**, 051003 (2007).
- Hillier, A. D., Quintanilla, J. & Cywinski, R. *Phys. Rev. Lett.* **102**, 117007 (2009).
- Youn, S. J. *et al. Phys. Rev. B* **85**, 220505(R) (2012).
- Friend, R. H. & Yoffe, A. D. *Adv. Phys.* **36**, 1–94 (1987).
- Lu, J. M. *et al. Science* **350**, 1353–1357 (2015).

PROTEIN PHYSICS

Forever ageing

Single-molecule techniques have long given us insight into the motion and interactions of individual molecules. But simulations now show that the dynamics inside single proteins is not as simple as we thought — and that proteins are forever changing.

Ralf Metzler

In the old school textbooks everything looked simple: biological cells were sacks full of water, with higher cells being furnished with internal organelles and a nucleus. Now we know that the cellular fluid is densely packed with large molecules such as proteins, ribosomes and RNA — and that they are highly structured^{1,2}. This crowding causes the diffusive behaviour of endogenous and foreign bodies to deviate from Brownian motion, be they granules, viruses or artificially introduced tracers^{3,4}. Perhaps more remarkable is the fact that even small proteins, such as green fluorescent proteins, diffuse anomalously at relevant timescales⁵, challenging our views of molecular information transfer in living cells. And now, writing in *Nature Physics*,

Xiaohu Hu and colleagues⁶ have revealed anomalous behaviour that challenges how we think about the internal dynamics of proteins.

On the level of single proteins, anomalous internal conformation dynamics have been known since ground-breaking bulk experiments on the rebinding dynamics of ligands to myoglobin⁷, eventually leading to the formulation of the known protein-folding models⁸. Sunney Xi's lab then managed to directly monitor the anomalous dynamics of the relative motion, $d(t)$, of two amino acids in a single protein — monomers that are chemically distant from one another along the molecule's backbone⁹ (Fig. 1).

From a modelling standpoint, one might view the internal dynamics of a

protein as similar to that of a polymer chain, despite differences in their typical shapes. In one of the simplest polymer models, the Rouse chain, consisting of point masses connected by harmonic springs, the effective random motion of a single monomer is anomalous (non-Brownian), yet Gaussian. Mathematically, the motion is described by a generalized Langevin equation with a power-law memory kernel, driven by Gaussian noise that is in fact power-law correlated thermal noise. The essential feature of this description is the stationary character of the process, that is, two-time correlation functions depend on time differences only, analogous to regular Markovian dynamics: no matter when we start a measurement with respect to the

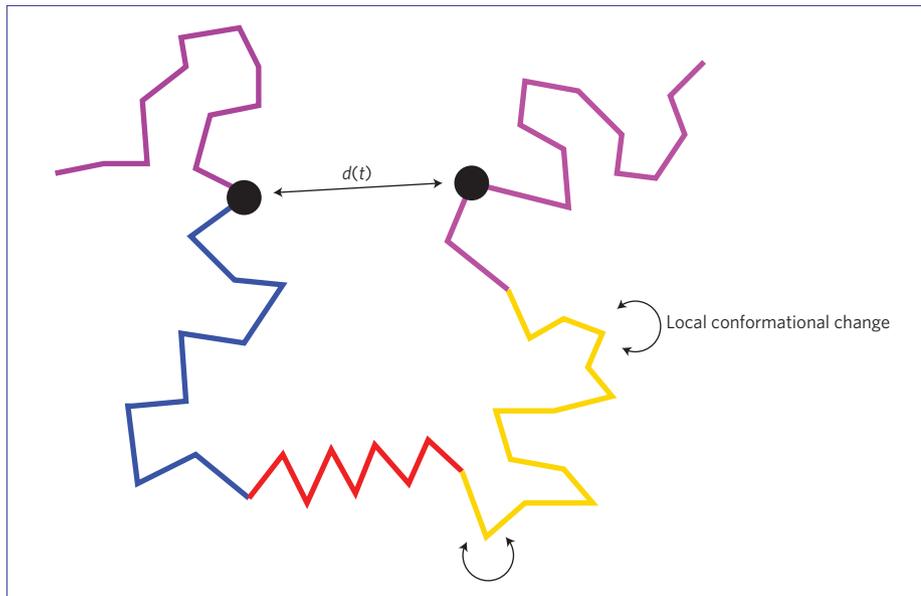


Figure 1 | The simulations of Hu *et al.*⁶ measure the relative distance $d(t)$ of two amino acids that are remote to each other in terms of the chemical co-ordinate along the protein backbone. Different colours schematically designate structural subunits of the protein molecule. Many local conformations, indicated by the small arrows, are necessary to effect the dynamics of $d(t)$.

initial preparation of the polymer, the result will turn out to be the same. It is often assumed that such stationary dynamics is also characteristic for the relative motion in proteins¹⁰.

The massive computer simulations by Hu *et al.*⁶ paint a vastly different picture for the different protein types studied. Resolving seven orders of magnitude in time by molecular dynamics techniques and combining this information with experimental single-molecule results, the authors demonstrated that the relative motion, $d(t)$, of chemically distant amino-acid pairs is self-similar over a range of 13 decades in time⁶.

Remarkably, the analysis reveals that this protein dynamics is non-stationary and exhibits ageing: in contrast to the simple Gaussian anomalous diffusion picture, the effective diffusivity characterizing the relative motion inside the protein becomes a decaying function of the observation time. Or, put differently, due to the non-stationarity of the correlation functions, the dynamics will appear different when we start our measurement at different delays after the original preparation of the molecule. For such processes, the ageing may lead to a population splitting¹¹: in the language of the relative motion of distal amino-acid pairs, some proteins may seem immobile during a finite measurement period, whereas others may show relative motion of varying activity. Concurrently, this type of dynamics has a strong memory of its initial distance $d(t = 0)$.

The authors presented a detailed analysis of this strange protein kinetics⁶. Namely, they showed how the intricate, fractal nature of the abstract network of the transition states of the entire molecule that they map out gives rise to a simple random-walk interpretation of the complex observed dynamics $d(t)$. One may interpret the relative motion of two amino acids in the language of the celebrated continuous-time random walk in a complex conformation space with infinite characteristic waiting time. The shape of the autocorrelation function of the relative motion, within measurement accuracy, follows the predicted incomplete beta function shape¹². This process is no longer Gaussian — curiously, this continuous-time random-walk model was also originally suggested to describe the Xie experiments⁹. Continuous-time random-walk anomalous diffusion violates the Boltzmann–Kinchin ergodic hypothesis and even long-time averages of an observable differ from the corresponding ensemble average¹².

The probed relative motion of a pair of chemically distant amino acids involves many local conformational changes of the protein (Fig. 1). These more global changes in the conformation are often relevant in the function of proteins. In the language of the rugged energy-landscape model of protein folding⁸, the observed continuous-time random-walk dynamics would mean that among many necessary conformational changes one or a few involve very deep

energetic traps. In the course of time, deeper and deeper traps are encountered, similar to quenched energy-landscape models for glassy systems¹³.

What information can we draw from the simulations and experiments for proteins in living cells? First, a caveat: in the cell's crowded environment, in which the observed protein is constantly rubbing shoulders with vicinal large molecules, the dynamics may be different to that of an isolated protein molecule. Conformations trapped in deep effective energy wells may be released due to massaging in the cellular environment. Hydrodynamic and charge effects in this interaction may further modify the ideal observations of an isolated protein.

However, given that the anomalous conformational dynamics found by Hu *et al.*⁶ prevails even in the *in vivo* environment, we may speculate whether this could indeed be beneficial for the cell and have a functional role. Namely, in an ensemble of proteins, some may rather quickly assume their function with a given distance of two chemically distant amino acids, whereas others remain close to their original distance $d(t = 0)$ and start their relative dynamics later. Simultaneously, such dynamics would lead to a larger spread of different stages of this time evolution of $d(t)$. Maybe such heterogeneity is important for certain, as yet unknown purposes. But even from a purely physical point of view, the findings by Hu *et al.*⁶ enrich our understanding: chemically distant amino acids exhibit non-Gaussian and non-stationary relative motion with an ageing character. □

Ralf Metzler is at the Institute for Physics and Astronomy at the University of Potsdam, D-14476 Potsdam-Golm, Germany.
e-mail: rmetzler@uni-potsdam.de

References

- Zhou, H. X., Rivas, G. & Minton, A. P. *Annu. Rev. Biophys.* **37**, 375–397 (2008).
- McGuffee, S. R. & Elcock, A. H. *PLoS Comput. Biol.* **6**, e1000694 (2010).
- Barkai, E., Garini, Y. & Metzler, R. *Phys. Today* **65** (8), 29–35 (2012).
- Höfling, F. & Franosch, T. *Rep. Prog. Phys.* **76**, 046602 (2013).
- Di Rienzo, C., Piazza, V., Grattton, E., Beltram, F. & Cardarelli, F. *Nature Commun.* **5**, 5891 (2014).
- Hu, X. *et al. Nature Phys.* **12**, 171–174 (2016).
- Austin, R. H. *et al. Biochemistry* **14**, 5355–5373 (1975).
- Frauenfelder, H., Sligar, S. G. & Wolynes, P. G. *Science* **254**, 1598–1603 (1988).
- Yang, H. *et al. Science* **302**, 262–266 (2003).
- Min, W., Luo, G., Cherayil, B. J., Kou, S. C. & Xie, X. S. *Phys. Rev. Lett.* **94**, 198302 (2005).
- Schulz, J. H. P., Barkai, E. & Metzler, R. *Phys. Rev. X* **4**, 011028 (2014).
- Burov, S., Metzler, R. & Barkai, E. *Proc. Natl Acad. Sci. USA* **107**, 13228–13233 (2010).
- Monthus, C. & Bouchaud, J. P. *J. Phys. A* **29**, 3847–3869 (1996).

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