

Exciting Insights

The newsletter dedicated to single-molecule spectroscopy

Hi there,

I hope you're doing well!

🎉 This month marks 30 years since one of the early papers that helped establish single-molecule FRET as a powerful tool for studying biomolecular dynamics. Since then, smFRET has transformed how researchers investigate conformational changes, molecular interactions, and complex biological processes.

To mark the occasion, we're hosting a special [Exciting Seminar](#) on 13 July exploring the evolution of smFRET over the past three decades and where the field is headed next.

We're delighted to be joined by Prof. Taekjip Ha, who made the very first smFRET measurement, for a discussion on the past, present, and future of smFRET.

Register below.

[Register now](#)

Curious to see how adding fluorescence correlation spectroscopy (FCS) and fluorescence cross-correlation spectroscopy (FCCS) to your current protocols and workflows, complementing your work to unlock hidden insights? [Download our new handbook](#) - a practical guide to FCS and FCCS.

More Exciting updates - including upcoming events, a new application note, and some FAQs - below 📌

Best wishes,

Tim
CEO and Founder of Exciting Instruments

Let's meet up

🇫🇷 [European South Atlantic Biophysics Congress](#) – 17th to 19th June – Montpellier, France

We'll be showcasing how accessible single-molecule spectroscopy can help researchers reveal real-time dynamics, interactions, and hidden heterogeneity in biomolecular systems.

Come visit us at our booth, where we will be presenting a poster and discussing applications in structural biology, biomolecular interactions and conformational dynamics. Take the opportunity to speak with our team about how the [EI-FLEX](#) can complement existing structural and biophysics workflows.

🇺🇸 [UCSC Cryo-EM Workshop](#) – 23rd to 26th June – Santa Cruz, California

We are proud to sponsor the 1st Edition Single Particle Analysis Workshop at UCSC this June. Focused on hands-on skills necessary to tackle complex biological questions using cryo-EM techniques, the EI-FLEX is a complementary technology that enables rapid, direct measurements of single molecules in solution, broadening access to conformational and dynamic insights. We will be on-site to support exploratory discussions and partnerships.

🇺🇸 [RNATx 2026](#) – 24th to 26th June – Worcester, Massachusetts

For decades, drug discovery chased proteins, but RNA therapeutics flip the script entirely. Instead of blocking a faulty protein after the damage is done, we can intercept the message *before it's ever translated*. From mRNA vaccines that rewired our pandemic response in record time, to siRNA silencing disease-causing genes with surgical precision, to antisense oligonucleotides reaching targets once considered "undruggable", RNA is proving to be the most versatile and programmable therapeutic platform biology has ever handed us.

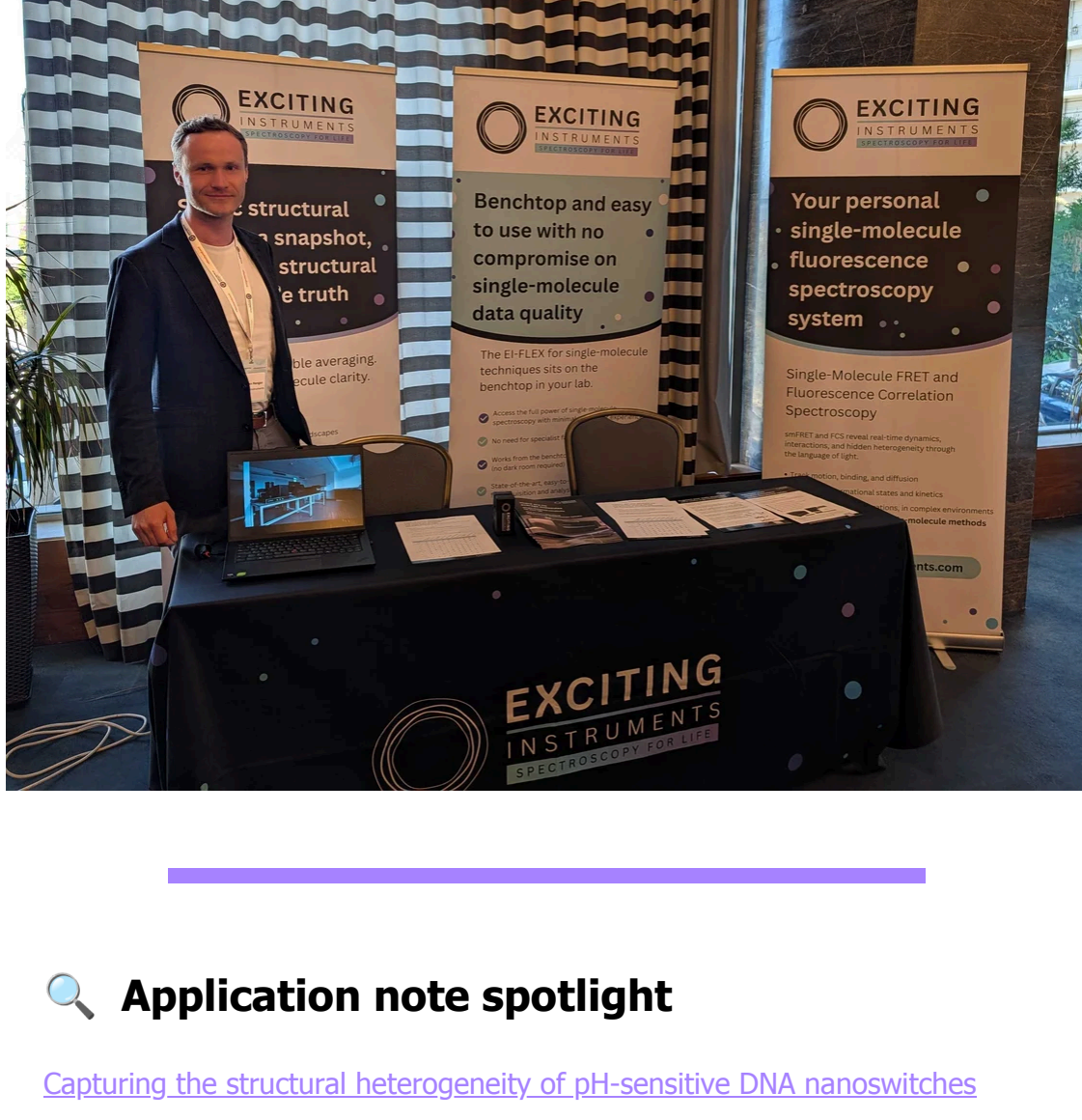
Drop by our booth at RNATx to learn how we've made single-molecule biophysical techniques accessible to all life science researchers with the introduction of the FLEX benchtop confocal fluorescence spectrometer. Study dynamics, conformational ensembles, and binding complexes of RNA and proteins in solution and even in real time to discern kinetic behavior! This type of data is an excellent complement to structural studies (e.g. cryoEM), molecular dynamics simulations, AI/ML predictions, as well as orthogonal biophysical approaches.

Looking forward to seeing you there and discussing the possibilities single-molecule analysis opens up!

🇺🇸 [The Protein Society Annual Symposium 2026](#) – 19th to 22nd July – Boston, Massachusetts

We were also proud to sponsor the 25th Annual Midwest DNA Repair Symposium at the University of Kansas Medical Centre at the end of May.

🔧 At Machines on Genes this week? Roman is on hand and ready to discuss how our easy-to-use tools allow you to assess the conformational dynamics and interactions of individual molecular machines. Be sure to say hello.



Application note spotlight

[Capturing the structural heterogeneity of pH-sensitive DNA nanoswitches](#)

This application note demonstrates how single-molecule FRET (smFRET) on the EI-FLEX was used to develop and characterise a pH-responsive DNA nanoswitch, revealing its conformational changes between open and closed states at picomolar concentrations.

The study shows that smFRET can accurately determine the nanoswitch's pKa and confirms that surface immobilisation preserves its pH-dependent switching behaviour.

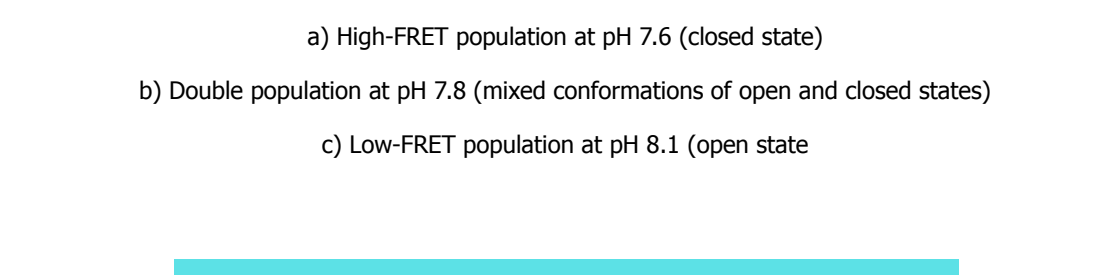


Figure 1 – smFRET demonstrates a pH-dependent shift in nanoswitch conformation
 a) High-FRET population at pH 7.6 (closed state)
 b) Double population at pH 7.8 (mixed conformations of open and closed states)
 c) Low-FRET population at pH 8.1 (open state)

FAQs - protein structure and dynamics

Here are some of the most commonly asked questions we hear from researchers exploring the potential of smFRET, FCS and FCCS in their work. For more information on protein structure and dynamics, check out [our application page](#).

- **Can FCS track the early stages of protein oligomerisation?**

As proteins begin to clump together (forming dimers, trimers, etc.), two things happen in FCS: the diffusion slows down, and the molecular brightness increases. If a dimer forms, the particle will be twice as bright as a monomer. This is an ideal technique for studying the early seeds of protein aggregates.

- **How does protonation or pH affect protein dynamics?**

Many proteins act as pH-sensors. By using smFRET, you can monitor how a protein's structure shifts between different states as you titrate the pH. This is vital for studying proteins that function in acidic environments, like lysosomes or the stomach.

- **Can I see domain swapping or hinge movements?**

Yes. Many proteins consist of multiple domains connected by flexible hinges. By placing the FRET pair across the hinge, you can measure the angular distribution of the domains and how they are influenced by the binding of substrates or cofactors.

- **Can I investigate how molecular chaperones affect protein dynamics?**

smFRET can capture how chaperones induce conformational shifts in target proteins. This is typically observed as a shift from a dynamic, broad FRET distribution of the unfolded protein to a narrow peak as a stable folded structure is induced. FCCS can also directly confirm whether a chaperone has bound a protein.

- **Can I use smFRET to study allostery?**

smFRET can show that binding a ligand at one site changes the structural dynamics at another distant location, such as an active site. This allows you to map the allosteric pathways that proteins use to regulate their own activity or track the allosteric effects of drugs.

Exciting company news

🎉 Congratulations to the Kaplan Lab at the Technion - Israel Institute of Technology on their recent installation of the EI-FLEX!

This was the first time we completed an install entirely remotely, which is a testament to the expertise of our team, the willingness of our customers to get stuck in, and the system's simplicity and ease of use. Looking forward to seeing all the great work to follow from the lab!



