FastHDX™, a Millisecond HDX-MS Platform

- FastHDX unlocks millisecond HDX-MS, delivering a 4-5 order-of-magnitude leap in labeling resolution and revealing fast, transient protein dynamics that conventional structural biology methods miss.
- Early adopter results from top pharmaceutical and academic institutions validate FastHDX for probing transient allosteric states in disease-relevant systems including diabetes, cancer, and Parkinson's disease.
- Seamless integration with standard LC-MS workflows, providing complete protein dynamics without requiring specialized infrastructure.

FastHDX is the first platform engineered to measure protein structural dynamics and conformational changes at millisecond resolution, enabling direct interrogation of transient states that are inaccessible with conventional techniques.

While many structural biology approaches focus on stable, folded proteins, a growing number of disease-relevant targets are often found through intrinsic disorder, weak interactions, and dynamic allosteric coupling rather than fixed structures. These proteins and regions populate transient conformational states that mediate low-affinity fragment binding and early regulatory events, yet remain difficult to interrogate with conventional techniques. Intrinsically disordered proteins and regions (IDPs and IDRs), defined as segments longer than 30 residues lacking stable structure, account for one-third of all eukaryotic proteins and play critical roles in diseases such as cancer and neurological disorders. Their highly dynamic nature has limited insight into the transient conformations that govern function and druggability. By enabling millisecond-resolved HDX-MS, FastHDX provides a direct experimental window into these short-lived states, allowing researchers to probe the dynamic mechanisms underlying intrinsically disordered biology and its therapeutic potential.

Key benefits of the platform include:

- Broad labeling time range (50 ms to 24+ hours) enables the capture of fast, transient conformational dynamics and long-timescale structural changes within a single platform, enabling comprehensive profiling.
- Millisecond labeling resolution (1 ms) enables researchers to resolve rapid protein motions and short-lived states that are invisible to conventional seconds-scale HDX-MS tools and techniques.
- Low sample consumption (8 µL total) enables millisecond HDX studies with limited or high-value samples, including peptides and early discovery targets.
- Automated analysis of up to 6 samples in triplicate with multiple time courses, with robotic expansion enabling up to 192 samples unattended.
- Seamless integration with commonly used LC-MS systems and analysis platforms for HDX-MS

enables the adoption of FastHDX without disrupting existing mass spectrometry infrastructure or retraining teams on entirely new workflows.

"FastHDX enabled us to capture millisecond-resolved exchange behaviour and quantify low-stability structural dynamics that are inaccessible with established HDX-MS approaches," said Jonathan J. Phillips, University of Exeter. "By resolving these fast processes, we can begin to connect protein dynamics with functional outcomes in ways that were not previously possible. As millisecond HDX-MS becomes more widely adopted, it will significantly expand how we study protein motion, disorder, and mechanism – ultimately unlocking our understanding of complex disease, biotechnology and medicines."

“While millisecond HDX-MS has existed in specialized academic settings, FastHDX is the first commercially available platform built to be robust, automated, and ready for real-world discovery workflows. That maturity is reflected in its adoption and evaluation by leading academic and pharmaceutical organizations, where the technology is being used to support advanced therapeutic development efforts."

FastHDX™：毫秒级氢氘交换质谱平台

- FastHDX 技术实现了毫秒级氢氘交换质谱分析，在标记分辨率上实现了 4~5 个数量级的飞跃，可揭示传统结构生物学方法无法捕捉的快速、瞬时蛋白质动力学特征。

- 全球顶尖药企与科研机构的早期应用结果证实，FastHDX 可用于解析糖尿病、癌症、帕金森病等疾病相关体系中的瞬时变构状态。

- 可与标准液相色谱-质谱（LC-MS）工作流程无缝衔接，无需专用配套设备即可完成完整的蛋白质动力学分析。

FastHDX 是首个专为毫秒分辨率下的蛋白质结构动力学与构象变化检测设计的平台，可直接解析传统技术无法触及的蛋白质瞬时状态。

众多结构生物学研究方法聚焦于稳定折叠的蛋白质，而越来越多疾病相关靶点的核心特征并非固定结构，而是固有无序性、弱相互作用与动态变构耦合。这类蛋白质及结构域会形成瞬时构象状态，介导低亲和力片段结合与早期调控过程，却难以通过传统技术研究。长度超过 30 个氨基酸残基、无稳定结构的**固有无序蛋白质/结构域（IDPs/IDRs）**，占真核生物蛋白质总量的三分之一，在癌症、神经系统疾病等疾病中发挥关键作用。其高度动态的特性，导致学界难以解析其调控功能与成药性的瞬时构象。而毫秒级分辨率的氢氘交换质谱（FastHDX），为研究这类短寿命状态提供了直接实验手段，助力科研人员解析固有无序生物学的动态机制及其治疗潜力。

fastHDX 氢氘转换质谱系统核心优势

- 标记时间范围广（50 毫秒~24 小时以上），单平台即可同时捕获快速瞬时构象动力学与长时程结构变化，实现全面表征。

- 毫秒级标记分辨率（1 毫秒），可解析传统秒级氢氘交换质谱无法检测的快速蛋白质运动与短寿命状态。

- 样品消耗量极低（总量 8 微升），适用于稀缺/高价值样品（包括多肽、早期药物发现靶点）的毫秒级氢氘交换研究。

- 可自动完成最多 6 份样品的 3 组重复与多时间点分析，通过机器人拓展可实现无人值守下 192 份样品的检测。

- 与主流氢氘交换质谱的 LC-MS 系统、分析平台无缝兼容，无需改造现有质谱设备、无需重新培训团队即可应用。

埃克塞特大学的乔纳森·J·菲利普斯表示：“FastHDX 让我们捕获到毫秒级分辨率的交换行为，定量解析了成熟氢氘交换质谱方法无法检测的低稳定性结构动力学。通过解析这些快速过程，我们得以将蛋白质动力学与功能结果关联，这是此前无法实现的。随着毫秒级氢氘交换质谱的普及，将极大拓展蛋白质运动、无序性与作用机制的研究范式，最终帮助我们攻克复杂疾病、生物技术与药物研发难题。”

“毫秒级氢氘交换质谱此前仅存在于专业科研场景中，而 FastHDX 是首个商用化平台，具备稳定、自动化的特点，可适配实际药物研发流程。该技术的成熟度已通过顶尖科研机构与药企的应用验证，正用于支持前沿治疗药物的研发工作。”