NMR BIOPHARMA SOLUTIONS

# Precision-built Peptide and Oligonucleotide Analytics

## TIDES Discovery and Development with NMR

Innovation with Integrity

### Introduction

Peptides and oligonucleotides (TIDES) are emerging as powerful drug candidates for various therapeutic areas due to their versatility, specificity and precision in targeting diseases like cancer, diabetes, cardiovascular diseases, genetic disorders, and rare diseases. Their regulatory considerations and structural complexity has created a high demand for accurate, robust, and high-resolution techniques to characterize these modalities.

Nuclear Magnetic resonance (NMR) spectroscopy is the gold standard for characterizing these molecules, including sequence verification, rational design, fragment-based screening, intermolecular interactions, stereochemical identification, batch-to-batch consistency, purity, and formulation quantification, ensuring compliance with the latest FDA and EMA guidelines.

**Therapeutic Areas**

Oncology
Diabetes
Cardiovascular Disease
Genetic Disorders
Rare Disease

## Peptides

NMR spectroscopy is redefining precision and performance for peptide characterization. Its ability to provide atomic-level structural detail ensures efficient and precise analyses for these vital therapies. Deeper understanding of therapeutic peptide structure enabled by NMR contributes to the development of safer, more efficacious, and higher quality products. The latest NMR technology allows for more time-efficient analyses to deliver products to the market quicker.

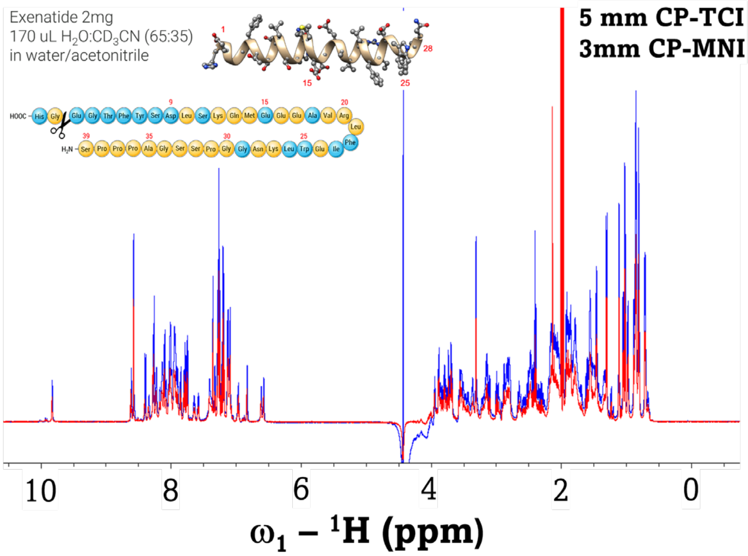



**Figure 1** 1D NMR spectra of exenatide comparing the latest probe technology

### Software Solution for Peptide Assignment

Leveraging the comprehensive analysis platform facilitates the full characterization of peptides:

- SOPs and integration into NMR automation for optimal data acquisition.
- Computer-assisted analysis and integrated structure and spectra display.
- Integrated state-of-the-art analysis tools and interfacing with external software packages

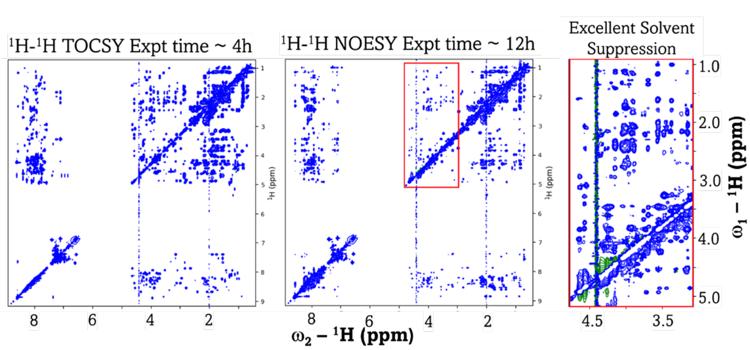



**Figure 3** 2D NOESY and TOCSY spectra for peptide assignment

### NMR Applications for Peptides

- **Structure Characterization**
  Defining the primary and higher order structure to support identity, stability, and comparability assessments.
- **Rational Design**
  Optimizing efficacy, stability, and off-target effects via guided sequence modifications.
- **Fragment-Based Screening**
  Identifying and validating binding interactions and mechanism of action.
- **Validation**
  Confirming identity and batch consistency.
- **CMC Support**
  Ensuring safety, efficacy, time-to-market, and regulatory compliance with high-resolution data through a Quality by Design approach.

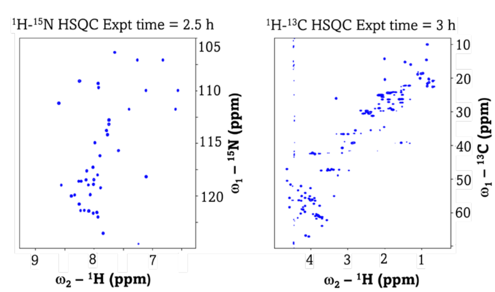



**Figure 2** Key 2D NMR spectra of exenatide at natural abundance

# Oligonucleotides

The efficacy of therapeutic oligonucleotides is directly linked to their structural complexity, from the stereoisomers to the dynamic behavior. Despite the inherent analytical challenges in addressing such complexity, NMR provides comprehensive and detailed structural insights of these innovative treatments.

Dive into the future of precision medicine with NMR's unparalleled capabilities!

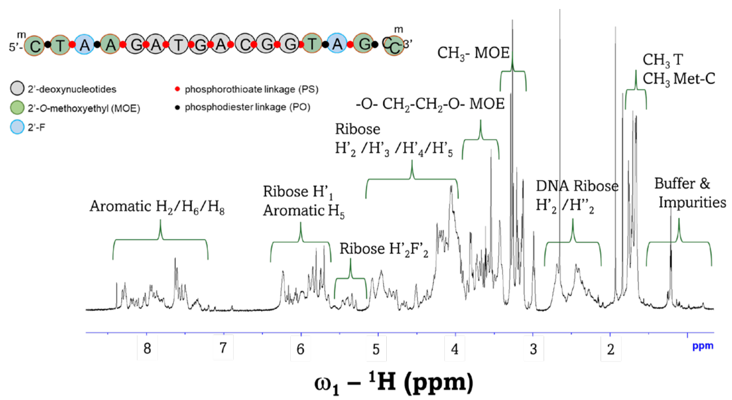



**Figure 4** 1D $^1$H NMR spectrum of therapeutic oligonucleotide

This cutting-edge technology is essential for accurately quantifying the PS/PO ratio in oligonucleotides, ensuring unparalleled accuracy and reliability.

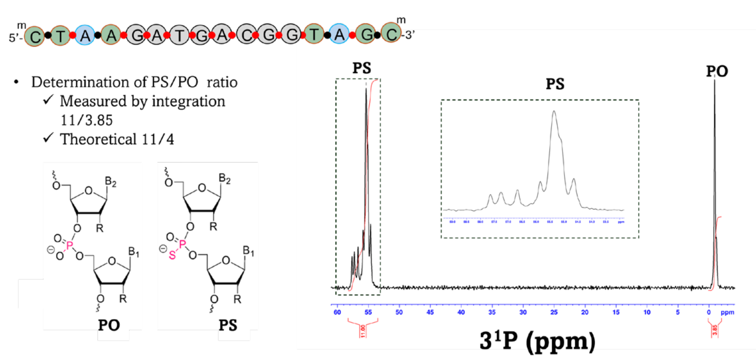



**Figure 5** PS and PO regions of the 1D $^{31}$P NMR spectrum

## Fingerprint of PS Region

- Distinctive pattern for $^{31}$P to $H_3$' $H_5$' correlations
- Accurate fingerprint
- Sequential Assignment partially possible

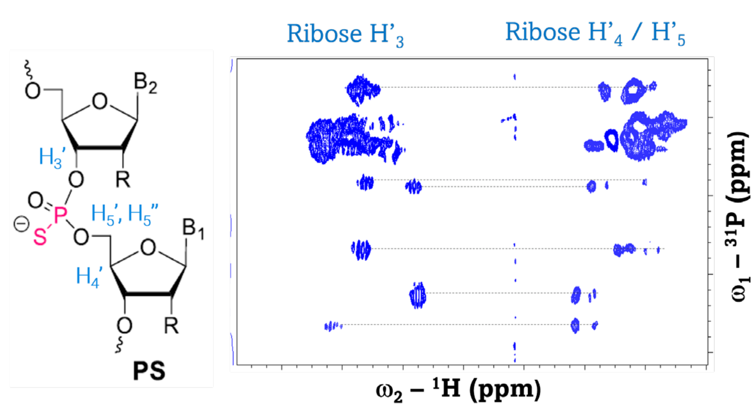



**Figure 6** 2D $^{31}$P NMR of therapeutic oligonucleotide at natural abundance

## NMR Applications for Oligonucleotides

- **Drug Development**
  Identifying and quantifying molecular interactions to optimize therapeutic efficacy.
- **Quality Control**
  Ensuring the purity and consistency of oligonucleotide-based drugs.
- **Structural Characterization**
  Determining the higher-order structure of oligonucleotides for better understanding of their function and stability.
- **Stereoisomer Identification**
  Distinguishing between different stereoisomers to ensure precise therapeutic targeting.

## Bruker's TIDES Solution

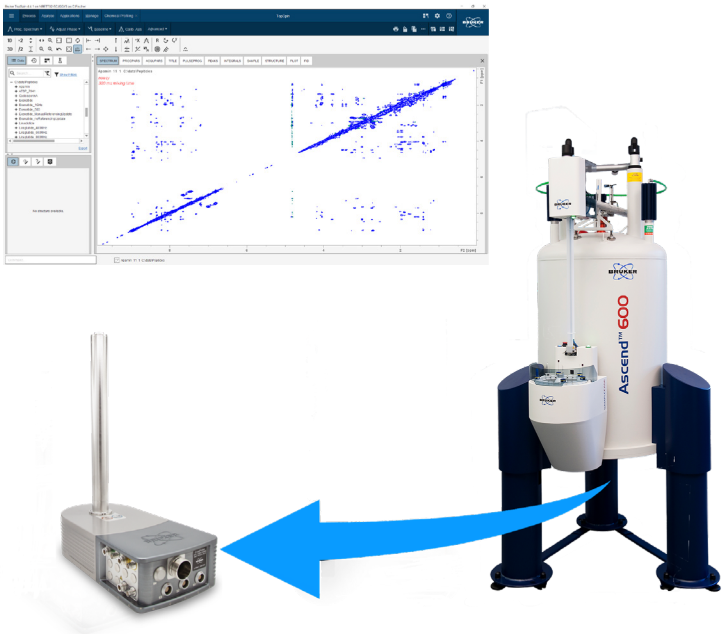
Set your lab up for success and confidently get your therapeutic TIDES to market quicker with the right NMR configuration to meet TIDES head-on. Bruker's 500 or 600 MHz NMR spectrometers deliver the sensitivity and resolution needed to generate high-quality data with less time than lower magnetic field strengths. The new Multi-Nuclear Inverse (MNI) CryoProbe delivers the necessary $^{1}H$, $^{13}C$, $^{15}N$, $^{19}F$, and $^{31}P$ resolution for:

- Detailed structural fingerprinting of peptides, including non-natural amino acids and higher-order structure.
- Precise $^{31}P$ profiling of oligonucleotide backbones, including phosphorothioate/phosphate (PS/PO) linkage ratios.
- Low-volume analysis with reduced solvent consumption and faster acquisition times—ideal for high-throughput workflows.

This configuration is purpose-built to meet regulatory expectations for identity, purity, and comparability, making it the gold standard for TIDES development and quality control.

**Bruker's TIDES Solution contains:**

- **Advanced Two-Channel Design:** Ultra-sensitive coil tunable to $^{1}H$ or $^{19}F$, offering 2x sensitivity gain and 4x faster measurements compared to 5 mm cryoprobes.
- **Multinuclear Capability:** Tunable to $^{13}C$, $^{15}N$, $^{19}F$, and $^{31}P$ for observation and decoupling, with sensitivity comparable to broadband cryoprobes
- **Eco-Friendly & Cost-Effective:** Uses one-third the deuterated solvents of 5 mm tubes.

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