# HFX(Y) Narrowbore Quad-resonance Probe with T3 Tuning for Efficient NMR of Solid Materials

## Technical Overview


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**All solid-state NMR experiments rely on high RF power, in order to obtain short pulse widths and high decoupling field strengths. The recent trend toward high-field magnets, with higher-frequency probes, along with the need for high RF power has created a technical challenge for probe design, which in the past has required physically large capacitors to be positioned in the magnet bore next to the sample. At the same time, the high cost of high-field magnets has put a premium on bore size. The solution to this problem has been Agilent's innovative Transmission Tuning Tube (T3) technology. This design is more efficient and compact at higher frequency, where power and space are at a premium. Replacing the tune and match capacitors with a transmission line moves bulky components outside of valuable bore space and improves efficiency. Broadband tuning is achieved by interchanging tuning tubes, each tunable over a range of frequencies. Multiple channels are achieved with multiple tubes, which are each long and narrow to fit in a narrow bore.**

**This technical overview illustrates several solid-state applications using the innovative Agilent HFX(Y) Quad-Resonance Narrowbore (NB) Probe, which can handle HX, FX, HF, HFX, and HFXY experiments, without changing probes. As with all recent Agilent solids probes, the new HFX(Y) probe uses Transmission Tuning Tube (T3) technology to obtain multiple channels in a narrowbore diameter and deliver quad-resonance $^{19}F$ spectroscopy to narrowbore magnets for the first time.**


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## The HFX(Y) NB probe

The existing Agilent HFX(Y) widebore probe has 4 ports for H / F / X / Y, individually. The H port is for $^{1}H$, F is $^{19}F$, X is $^{13}C$ - $^{31}P$ and Y is $^{15}N$-$^{13}C$. For the narrowbore HFX(Y) probe, H and F are combined into one port, using a new "Split" capability which enables dual tuning of the highband port. The HFX(Y) probe therefore requires only 3 ports (H, F / X / Y), providing four-nucleus capability in the limited diameter of the narrowbore probe. The highband tuning tube has three knobs, "Tune", "Match", and "Split" (Figure 1), to provide tuning of H and F. The Split knob changes the frequency separation between the H and the F tuning dips. The Tune and Match knobs affect both dips together.

As with the HX(Y) probe, which can be converted to HX, the Y channel of the HFX(Y) probe is removable to produce an HFX tuning configuration with better signal-to-noise. As with any T3 probe, the HFX(Y) probe can also accommodate the addition of Agilent's Low-gamma Box to tune nuclei below $^{15}N$. The HFX(Y) probe is a versatile probe for many experiments, whether or not they involve $^{19}F$.

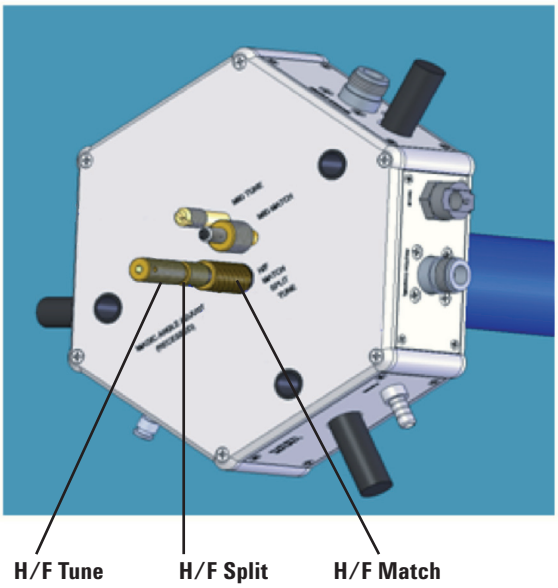


*Figure 1. Location of the Tune, Match and Split knobs on the HFXY probe. A HF combiner, containing bandpass filters, is supplied separately. It is required when both RF channels are irradiated, to combine H and F channels into one at the probe and isolate them at the amplifiers and receivers.*

Figure 2 shows the system diagram of the probe and its connections to an Agilent NMR system, including an HF combiner, bandpass filters, directional couplers and pre-amplifiers. The combiner and filters are provided together in a separate unit. The combiner typically joins transmitters #1 and #3 and is followed by series directional couplers for these two channels. This probe is compatible with the new Agilent DD2 console at 400, 500 and 600 MHz, as well as earlier NMR systems, having the required number of channels. High-power amplifiers for the highband channels are recommended in many cases, depending on the rotor size, but are not required.

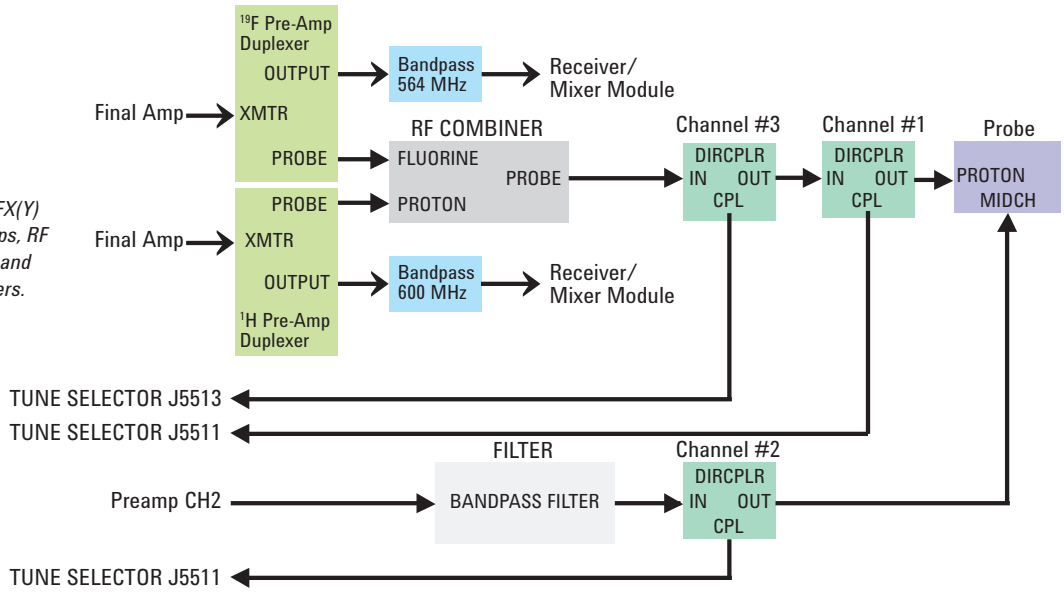


*Figure 2. System diagram of the HFX(Y) NB probe, preamps, RF combiner, filters, and directional couplers.*

## New “trtune” capability with VnmrJ 3.1 software

The VnmrJ3.1 software provides a new easy-to-use tuning procedure that enables simultaneous display of multiple channels. It is necessary to display both H and F tuning simultaneously when using the HFX(Y) probe in order to avoid the need to switch back-and-forth between the H and F tuning displays when adjusting the “split”.

The trtune software shows the tuning displays of up to 5 channels simultaneously, with the center frequency of each tuning display lined up, similarly to a spectrum analyzer or multichannel scope. To tune, one lines up all the tuning dips at the center. The trtune tuning software (Figure 3) is a useful tool not only for the HFX(Y) probe, but all manually tuned probes, including those for liquid state NMR. It is compatible with the Agilent DirectDrive consoles, VNMRS and DD2.

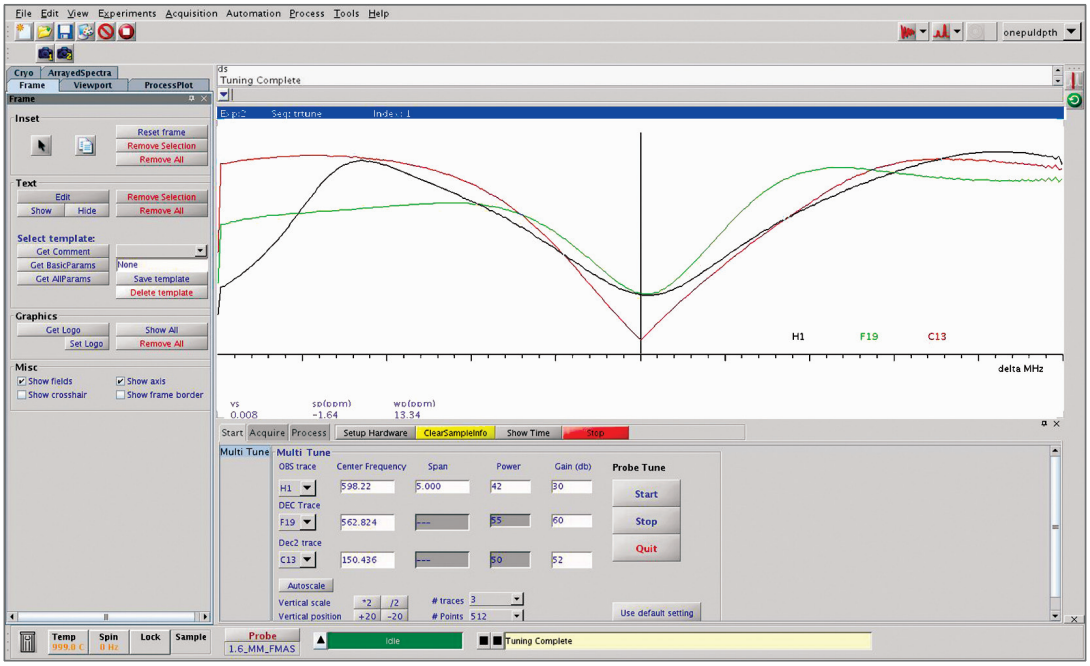


*Figure 3. The trtune panel in VnmrJ3.1 software. The probe is correctly tuned and matched when the three dips are centered on the horizontal axis, and the dip extends as far as possible down the vertical axis.*

## A wide range of applications

All spectra presented here were acquired by an Agilent VNMRS 600MHz NB using a new 1.6 mm HFX(Y) NB MAS probe with Vespel spinning module installed. The spectrometer was equipped with two 100W amplifiers for H and F channels, and two 300W amplifiers for broadband channels.

### *Polymer $^{1}H$-$^{19}F$ analysis*

Fluoropolymers are widely used for microelectronic devices, because they display excellent properties such as high thermal stability and good resistance to organic solvents. Polyvinylidene fluoride (PVDF) is one of the most common fluoropolymers.

Figure 4 shows $^{19}F/^{1}H$ cross-polarization magic-angle spinning (CPMAS) spectra and $^{19}F$ direct-polarization magic-angle spinning (DPMAS) spectra of PVDF. Normally polymers contain crystalline and amorphous regions, and how they mix determines the character of the material. It is well known that the crystalline region is emphasized by CPMAS spectra because of the strong dipolar coupling. Therefore, by comparison of CPMAS and DPMAS, crystalline and amorphous regions in the polymer can be distinguished easily. Comparison of the $^{19}F$-DPMAS and $^{19}F/^{1}H$-CPMAS spectra in Figure 4 illustrates that the peaks at -90 ppm and -135 ppm are in the amorphous regions, and the -70 ppm and -100 ppm peaks are in crystal regions.

Figure 5 shows $^{13}C/^{1}H$-CPMAS and $^{13}C/^{19}F$ -CPMAS spectra, which were observed with both $^{1}H$ and $^{19}F$ decoupling . These spectra demonstrate that signals for $^{13}C$ that are close to $^{1}H$ or $^{19}F$ are easily assigned by observing the $^{13}C$ signal under high resolution using simultaneous {$^{1}H$, $^{19}F$} decoupling. If the probe was not double-tuned for $^{1}H$ and $^{19}F$, only one of the two nuclei could be decoupled at a time, making it very hard to obtain high resolution spectra.

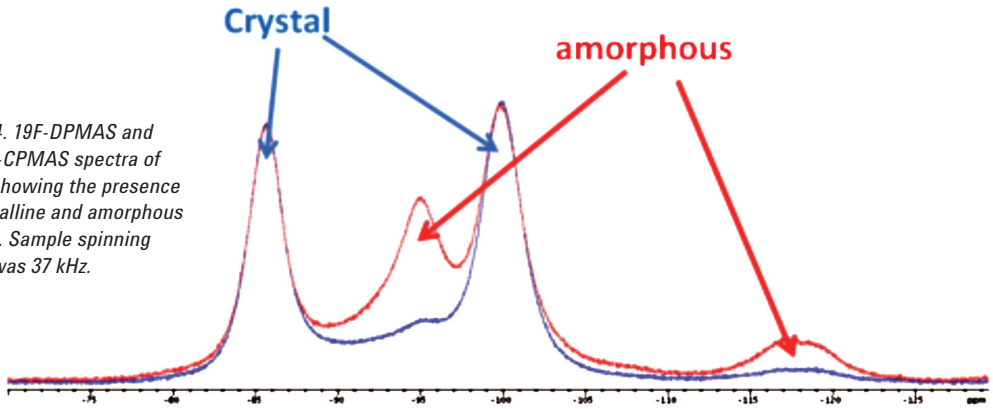


*Figure 4. 19F-DPMAS and 19F/1H-CPMAS spectra of PVDF, showing the presence of crystalline and amorphous regions. Sample spinning speed was 37 kHz.*

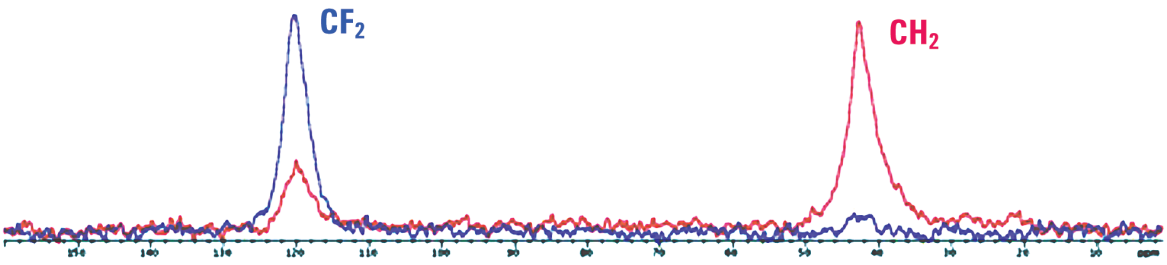


*Figure 5. 13C/1H-CPMAS and 13C/19F-CPMAS spectra of PVDF. Sample spinning speed was 37 kHz. A contact time of 100 µsec was applied in order to obtain only the proton or fluorine directly coupled carbon spectrum.*

### *Pharmaceutical $^{13}C$-$^{19}F$ analysis*

Pharmaceutical products are primarily solids, and many of them have more than one drug form, as is often the case in amorphous, polymorphic, solvated, and co-crystalline substances. Solid-state NMR is a powerful technique for the analysis of different drug forms in pharmaceutical products. $^{13}C/^{1}H$-CPMAS of different polymorphic forms can provide information about the crystallographically inequivalent sites, and about the molecular conformations.

Some pharmaceutical samples contain not only abundant protons but also fluorine. In order to obtain high resolution $^{13}C$ spectra with such samples, it is necessary to decouple both $^{1}H$ and $^{19}F$ during the acquisition period. Triamcinolone is a fluorine-containing corticosteroid drug. Figure 6 shows the $^{13}C/^{1}H$ CPMAS spectra of triamcinolone acetonide with simultaneous $^{1}H$ and $^{19}F$ decoupling, using various decoupling powers for $^{19}F$ at 37 kHz sample-spinning speed. Low power $^{1}H$ decoupling (only 9 kHz) was applied during acquisition, because of the fast sample-spinning speed. Under $^{19}F$ non-decoupling, the $^{13}C$ peak, which is directly connected to $^{19}F$, is split in two (denoted by the red circle in Figure 6). The splitting width is exactly the same as $J_{CH}$, a value which is known to be 177 Hz. Therefore, it is explicit that the $^{13}C$-$^{19}F$ dipolar interaction was averaged out by the 37 kHz sample spinning, and only the $J_{CH}$ coupling was observed. With increasing $^{19}F$ decoupling power, the Rotary Resonance effect was observed and the carbon peak at 102 ppm was broadened at the $n \times \omega_r = \omega_1$ condition.

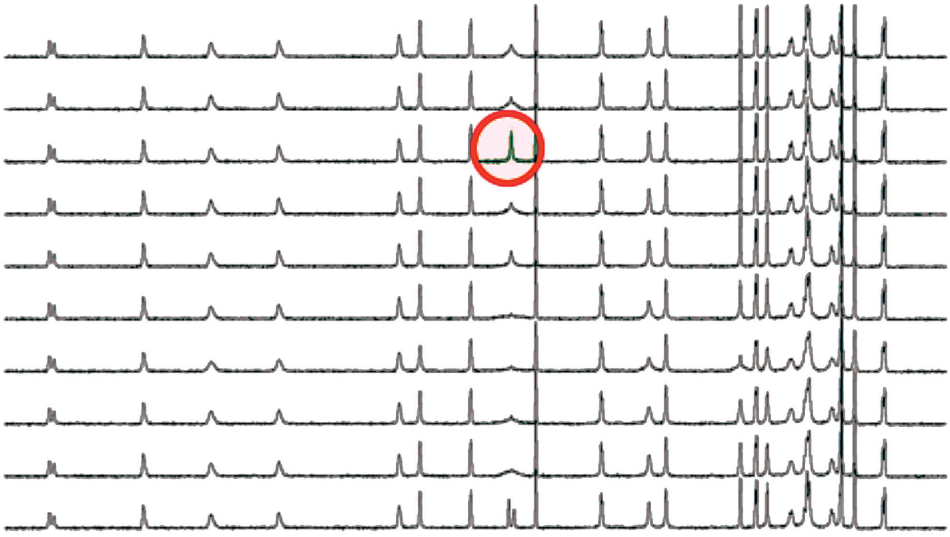

*Figure 6. $^{13}C/^{1}H$-CPMAS of triamcinolone acetonide with varying 19F decoupling powers from 0 kHz (bottom) to 94 kHz (top). Sample spinning speed was 37 kHz, recycle delay 5 sec and contact time 3 msec.*

### *Biomaterial $^{1}H$-$^{19}F$-$^{31}P$ analysis*

The study of biomaterials is becoming one of the most significant areas for solid-state NMR analysis. Hydroxyapatite is widely used as a dental and medical implant material, because it is similar to the tooth and bone mineral apatite in chemical composition and structure. It also has excellent bioactivity. Derivatives of hydroxyapatite find various applications in chemical sensors, absorbents for protein separations and catalysts.

Figure 7 shows $^{31}P/^{1}H$ and $^{31}P/^{19}F$ CPMAS spectra with $^{1}H$ decoupling of a fluorine-substituted hydroxyapatite. A $^{31}P/^{1}H$ CPMAS spectrum, has a three-times broader line width than a $^{31}P/^{19}F$ CPMAS spectrum. The $^{31}P$-$^{1}H$ dipolar interaction is stronger than that for $^{31}P$-$^{19}F$ because of the distance between the two nuclei, and here $^{19}F$ decoupling was not needed. Because of the broader line with $^{19}F$ CPMAS, we can conclude that the $^{31}P$ nuclei which are close to $^{1}H$ have a greater chemical shift dispersion than those that are close to $^{19}F$.

Figure 8 shows a two-dimensional (2D) $^{19}F/^{1}H$-heteronuclear correlation (HETCOR) spectrum of a fluorine-substituted hydroxyapatite sample. As the sample spinning speed is 36 kHz, a homo-decoupling pulse scheme for $^{1}H$, such as FSLG (Frequency-Switched Lee-Goldberg), was not needed during the evolution period. Many cross peaks in the 2D spectrum indicate that there are several different correlations between proton $^{1}H$ and fluorine $^{19}F$ nuclei in the molecule, revealing multiple fluorine sites.

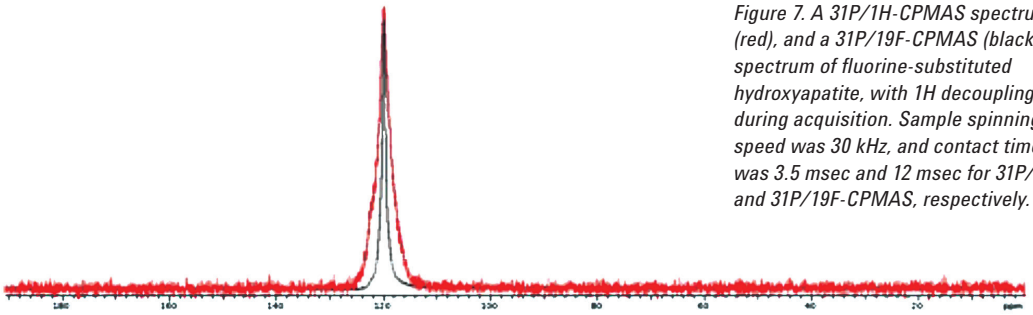

*Figure 7. A 31P/1H-CPMAS spectrum (red), and a 31P/19F-CPMAS (black) spectrum of fluorine-substituted hydroxyapatite, with 1H decoupling during acquisition. Sample spinning speed was 30 kHz, and contact time was 3.5 msec and 12 msec for 31P/1H and 31P/19F-CPMAS, respectively.*

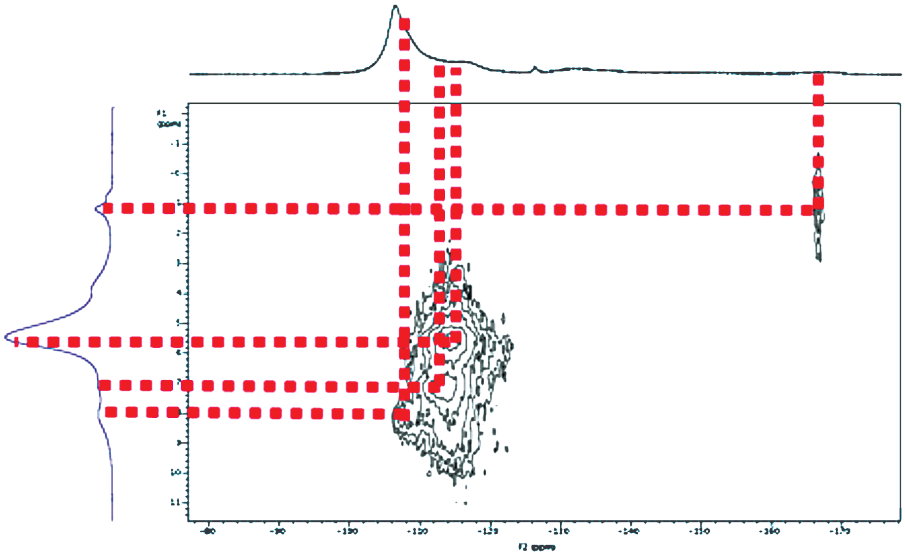

*Figure 8. 19F/1H-heteronuclear correlation (HETCOR) spectrum of a fluorine-substituted hydroxyapatite. Sample spinning speed was 36 kHz. Contact time was 8 msec.*

## Conclusions

The new Agilent HFX(Y) Quad-Resonance Narrowbore (NB) Probe with T3 tuning provides the ability to perform HX, FX, HF, HFX, and HFXY experiments without changing probes. The unique T3 tuning makes nearly all NMR sensitive nuclei available for analysis and enables the use of narrowbore magnets, reducing the cost as well as the space requirement. The new trtune easy-to-use tuning procedure in VnmrJ3.1 software provides for optimal use of the HFX(Y) probe, by enabling simultaneous display of up to 5 channels. The new HFX(Y) probe can be used with many of the Agilent NMR systems to provide critical structural information about a variety of solid materials, including polymers, pharmaceuticals and biomaterials.

## Acknowledgement

The author wishes to thank Dr. Junko Kikuchi, Shionogi & Co., Ltd. for kindly providing a triamcinolone acetonide sample.

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Published in USA, April 8, 2011
Publication Number 5990-7859EN

Agilent Technologies