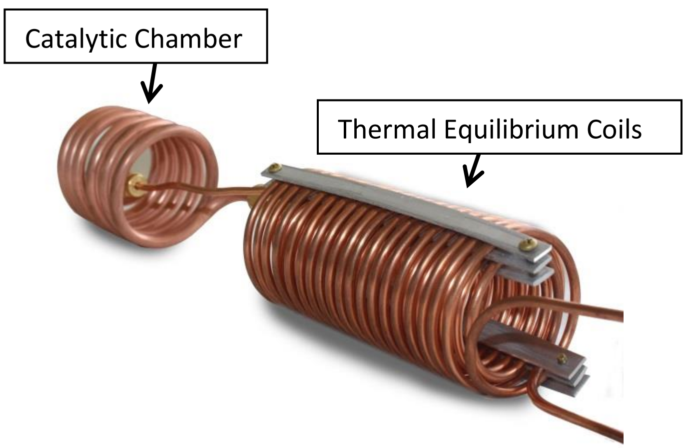
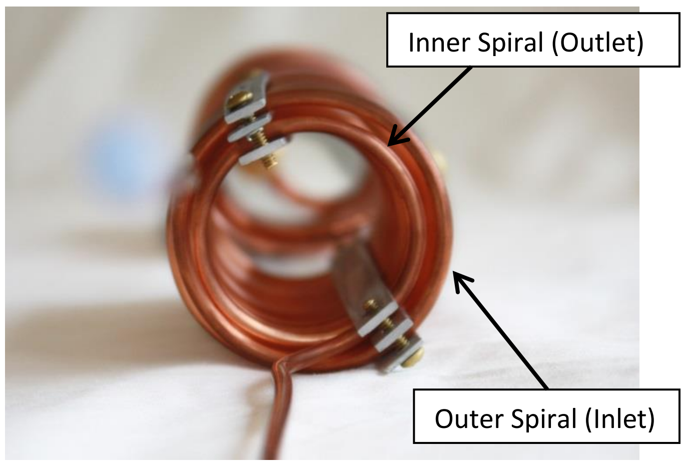
Para-Hydrogen Flow Cryostat Operating Instructions

<u>Para-Hydrogen (PH2) Flow Cryostat Description:</u>

The cryostat consists of 2 segments. The lower segment made of 1/4" Tubing houses the catalyst and is the part which is submerged in liquid nitrogen during its use. The Upper segment consists of 2 spirals (one inside the other) made of 1/8" tubing. The functions of these spirals are for temperature regulation of the Hydrogen gas.

Gas Inlet: The inlet of gas is designated as the *<u>Outer Spiral</u>*. Incoming gas will enter the catalytic chamber at the bottom of the spiral first, the make its way up the catalytic chamber, and exiting through the upper Inner Spiral.
Gas Outlet: The polarized gas will exit the Catalytic chamber via the upper *<u>Inner Spiral</u>*.





Prior to using the flow cryostat for the first time, it must first be purged with either Ultra High Purity Hydrogen or for 20 minutes to ensure that all moisture in the system has been removed. Moisture inside the cryostat will affect its performance. <u>Purged gas should be vented to a fume hood for safety</u>.

Subsequent uses after initial purging and leak and pressure test require purging prior to every use.

Initial Bench Top Testing: Prior to being used for the first time, initial bench top testing and purging is required to ensure that the unit is free from defects that could have occurred during shipping.

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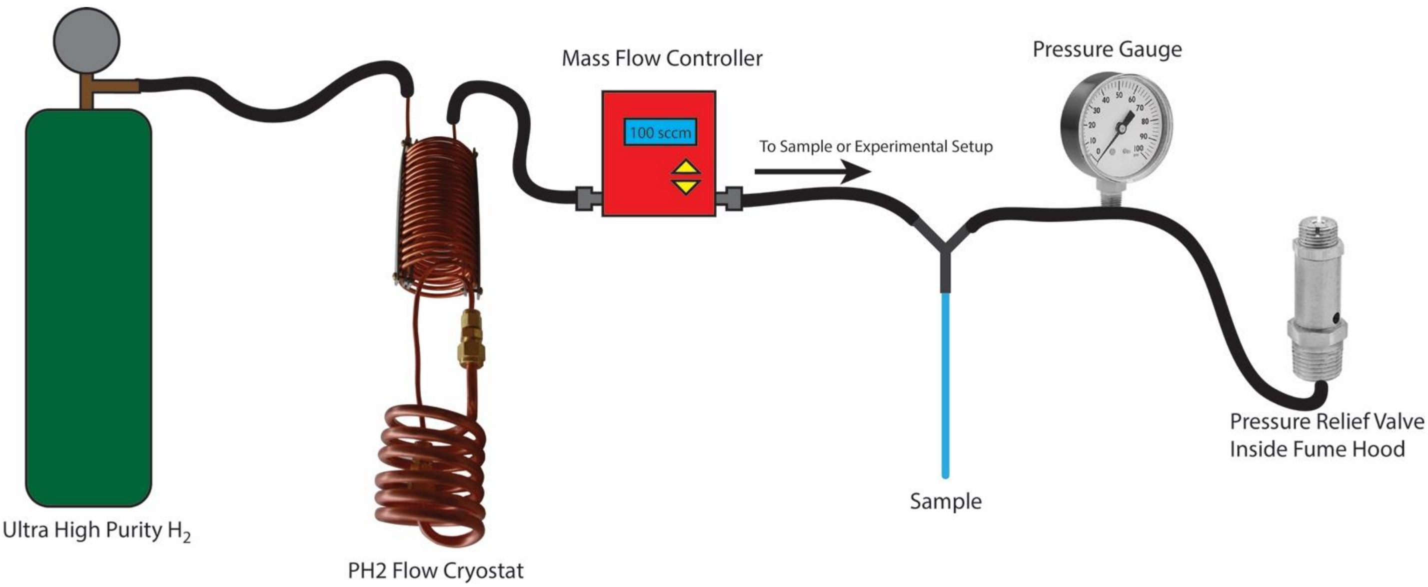
Connecting Your Flow Cryostat



The figure above displays a typical experimental setup. For Initial Bench Top purging and testing, the sample is not required. Furthermore, for this bench top testing no cryogen is required.

- Assemble your setup, as displayed above without the Sample connected. Use the appropriate connectors to connect all gas lines to the Cryostat, Mass Flow Controller, Pressure Gauge, and Pressure Relief Valve. Recommended Gas Lines from your Hydrogen Gas Cylinder to your Mass Flow Meter should be 1/8" Copper Tubing. Teflon lines can be used after the MFC.

  The Adaptors on your Mass Flow Meter should also be Brass with the appropriate NPT fitting. Most MFCs utilize 1/8 NPT thread. A preferred fitting on the Inlet side should be:
  https://www.mcmaster.com/5272k292
  and, subsequently on the outlet side to enable you to connect 1/8" Teflon tubing:
  https://www.mcmaster.com/5779k102

- The Cryostat is operated at pressures between 50 to 100 PSI depending on the end users requirements. Thus, the appropriate pressure relief valve should be used. We Recommend these Pressure Relief Valves and Push to Connect Adaptor:
  https://www.mcmaster.com/9889k15-9889K608
  https://www.mcmaster.com/5779k123

- Xeus Technologies does offer a complete solution: PH2 Bubbling Manifold System, complete with MSC, connectors, sample tubes, pressure gauge, valves, and pressure relief valves. Contact us for more information.

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Moisture Purging and Pressure Leak Testing

- Both these Tests can be accomplished at the same time. In other words, while you are purging the system of moisture, you should be performing the Pressure Leak Testing.

Moisture Purging:

- Once all connections are made, set your Tank Pressure to slightly above the pressure of Pressure Relief Valve rating. For Instance, if using a 50 PSI Relief Valve, then set your Gas Cylinder regulator outlet pressure to 60 PSI. The Pressure Relief valve should be placed inside the fume hood.
  NOTE: Do Not Exceed your MFCs recommended Maximum Pressure Rating, as this could result in damage of the unit.

- Set your MFCs Flow Rate to your desired flow (100 sccm to 150sccm), and begin flowing Ultra High Purity Hydrogen gas. The system must be purged of all moisture and other atmospheric gases, thus it is highly recommended you Hydrogen which will be used for your experiments. The System should be purged for at least 20 minutes.

Pressure Leak Testing:

- To accomplish this test you will need Leak Detector such as:
  - Snoop Leak Detector: From Swagelok , or Sigma Aldrich. Other Vendors also carry this brand.
  - Other commercial available brands: https://www.mcmaster.com/1012t18
  - Or you can simply make you own by mixing dish shop with water inside a lab squeeze bottle.

- Apply Leak Detection Liquid to all connectors on your setup. If there is a leak, the applied liquid will start generating bubbles.
  - **Brass Compression Fittings:** If you detect any such leaks, tighten the fitting to resolve the leak. If Leaking persists after tightening, the tube and ferrule may not have been compressed correctly. In such cases, the tube will have to be cut and a new ferrule installed, and then retightened.
  - **Push to connects:** If leaks are detected from these fittings, these are usually caused by the Teflon tubing not being cut straight or being deformed. Simply cut off the bad segment and attach again. If leaking persists, the connector may be defective and needs to be replaced.
  - **NPT Thread Connectors:** Teflon Tape must be applied to the threads before installing. If Teflon tape is not applied, then the chance of leaking increases. If leaking is detected and not resolved by tightening the fitting, then Teflon tape should be re-applied to the thread and re-installed.

- You must ensure that your pressure gauge located after your sample (PH2 exit path to fume hood) is reading the same pressure as the rating of your selected pressure relief valve. If you are detecting a much lower pressure (i.e Pressure Relief Valve Rating = 50 PSI and Pressure Gauge is measuring 40 PSI), then this is an indication that you have a pressure leak in your setup. Use the Leak Detector to find the leak and subsequently remedy the leak.

- There are 4 connections on the Flow Cryostat which need to be tested to make sure there are no gas leaks. See the figure below for their location.

Catalyst activation

NOTES: If the catalyst is not activated, the highest production rate should not exceed 150 sccm. Otherwise, the parahydrogen fraction may be substantially less than 50%.
Catalyst activation is required according to the manufacturer's specifications https://www.molecularproducts.com/wp-content/uploads/2017/02/OP-Catalyst-166_Rev-D_Technical-Datasheet_OP-Catalyst.pdf
In practice, the catalyst activation can be performed under hydrogen flow conditions (ca. 150 standard cubic centimeters per minute (sccm)) with application of a heat gun. The heat should be applied evenly to the catalyst-containing spiral for at least 15 minutes. Do not overhead the catalyst chamber to more than 200 C. If in doubt, activate longer but at lower operating temperature.

Recommended Operating Parameters

NOTES: The tested by us flow rate is up to 1,000 standard cubic centimeters per minute (sccm) of H_2 flow after catalyst activation (without any degradation of parahydrogen fraction). Higher flow rates likely can be potentially employed – our spiral contains ~20 gram of catalyst – according to vendor's specifications, up to 1,200 sccm per gram of catalyst is feasible (using fully activated catalyst) corresponding to 24,000 sccm.

The Dewar must be filled with at least ~13cm height of Liquid Nitrogen to ensure that the catalytic chamber is immersed completely for proper operation. The thermal exchange upper coils may or may not be contact with liquid nitrogen.

Para-Hydrogen Conversion Quantification Protocol

The parahydrogen quantification has been previously described. For complete details please refer to the following literature:

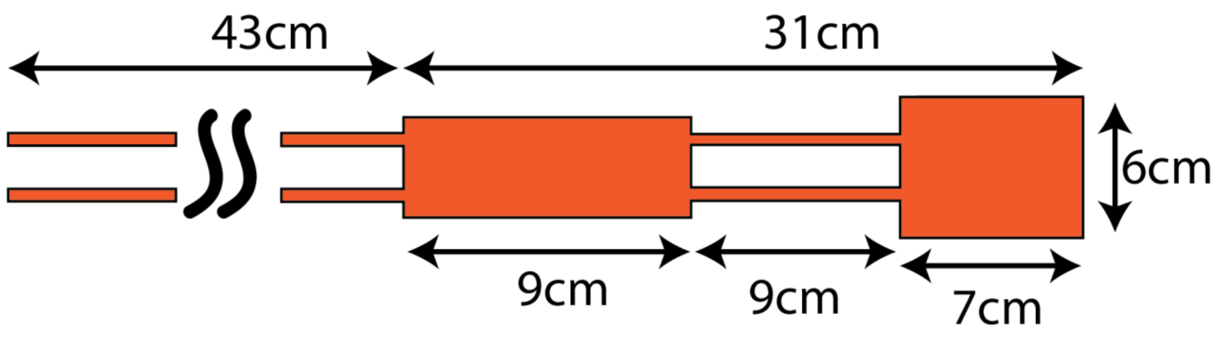
1) Feng, B.; Coffey, A. M.; Colon, R. D.; Chekmenev, E. Y.; Waddell, K. W., A pulsed injection parahydrogen generator and techniques for quantifying enrichment. *J. Magn. Reson.* **2012,** *214*, 258-262.
2) Birchall et al. High-Pressure Clinical-Scale 87% Parahydrogen Generator. *Analytical Chemistry* **2020** (under review).
3) Hövener, J.-B.; Baer, S.; Leupold, J.; Jenne, K.; Leibfritz, D.; Hennig, J.; Duckett, S. B.; von Elverfeldt, D., A continuous-flow, high-throughput, high-pressure parahydrogen converter for hyperpolarization in a clinical setting. *NMR Biomed.* **2013**, *26* (2), 124-131.
4) Shchepin et al. *Analytical Chemistry* **2021** (in preparation).

Briefly, hydrogen gas is filled in 5-mm NMR tube by flowing gas in the tube via 1/16" OD or 1/8" OD tubing for over a minute. The NMR tube is capped with a cap. Two-three samples are filled with normal hydrogen and parahydrogen-enriched mixture. NMR spectra (no shimming or lock) are recorded using high-resolution NMR spectrometer with the following parameters: 90-degree flip angle, repetition time: 50-100 ms, acquisition time: 25-50 ms, number of scans: 256-512, line broadening: 10-50 Hz. The signal integrals (from enriched sample and unenriched (*i.e.*, normal) H_2 samples are compared to compute the fraction of parahydrogen in the parahydrogen enriched mixture using the following equation:

$$f = 1 - \frac{3(enriched\ Signal)}{4(unenriched\ Signal)}$$

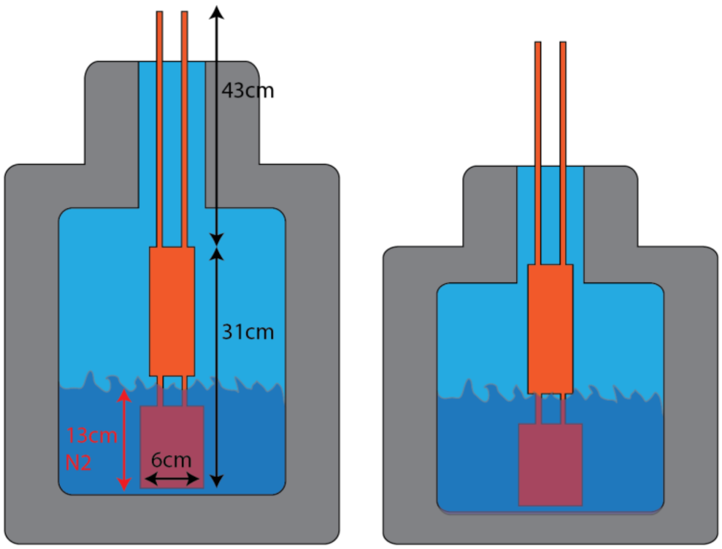
Choosing a Liquid Nitrogen Dewar

Dimensions of each Cryostat may very slightly. The schematic representation (not to scale) lists the approximate dimensions of the cryostat.



When selecting a Dewar to meet your needs, you must ensure that the mouth of the Dewar is wider than 6cm to allow the Cryostat to be lowered inside during its use. For the Dewar to be sealed with a Foam

Lid/Cap, the main body (~31cm) must have enough clearance from the mouth of the Dewar to be able to seal properly. Both representations in the figure below are acceptable. A custom dense foam sealing cap with feed through holes for the cryostat gas inlet and outlet tubes can be made once all critical dimensions of the chosen Dewar are known.



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