

## **Answers to comments**

*Open-source, partially 3D-printed, high-pressure (50 bar)  
liquid-nitrogen-cooled parahydrogen generator*

**mr-2020-27**

Frowin Ellermann et al.  
December 14th, 2020

# 1 SC1: Igor Koptug

**Referee comment:** From the title, I had an impression that the generator or at least its essential parts were 3D-printed, which, as I found later, was not the case. I believe it may be a good idea to refine the paper title.

**Answer:** We understand that the title could be misleading and to avoid it the new title reads as "Open-source, partially 3D-printed, high-pressure (50 bar) liquid-nitrogen-cooled parahydrogen generator"

**Referee comment:** As always, I'm advocating the spelling of "parahydrogen" and "orthohydrogen" as single words without a dash, which I believe is the only correct way to spell them (cf. paratrooper, parabola, orthophosphoric acid; also in dictionaries, e.g., <https://www.thefreedictionary.com/parahydrogen>).

**Answer:** We understand your point and removed the dash. Additionally, we stick to the non-italic form.

**Old text:** "para-hydrogen"

**New text:** "parahydrogen" throughout the text

**Referee comment:** The word "allotrope" in the reference to parahydrogen is acceptable in the historic context, but in fact is incorrect. By definition, allotropy is the existence of a chemical element in two or more forms, which may differ in the arrangement of atoms in crystalline solids or in the occurrence of molecules that contain different numbers of atoms (e.g., graphite, charcoal, diamond, fullerenes). Parahydrogen is this not an allotropic form of H<sub>2</sub> but rather its nuclear spinisomer.

**Answer:** We changed the word allotrope/allotropic to "nuclear spinisomer" except for the citation and the text referring to it.

**Old text (e.g.):** "The spin of hydrogen nuclei (proton) is the origin of the two allotropic forms or two spin isomers of hydrogen."

**New text:** "The spin of hydrogen nuclei (of protons) is the origin of the two nuclear spinisomer forms of dihydrogen."

**Referee comment:** line 40, naphthalene derivative (Stevanato et al., 2015) cannot be classified as spin isomer as it is not symmetric, so that the generalized Pauli principle is not applicable to it. 5) Line 39, water (Mammoli et al., 2015; Meier et al., 2015) was not enriched in the Mammoli paper experiments, or at least could not be extracted to RT. A better reference to

spin isomers of free water would be to the molecular beam separation experiments (e.g., doi: 10.1126/science.1200433 or 10.1021/acs.jpca.9b04294).

**Answer:** We rephrased the sentences and added proposed references.

**Old text (e.g.):** "Hydrogen is not the only compound that has stable or long-lived spin isomers at room temperature (rt) there are many examples: deuterium (Knopp et al., 2003), water (Mammoli et al., 2015; Meier et al., 2015), ethylene (Zhivonitko et al., 2013), and even naphthalene derivative (Stevanato et al., 2015)."

**New text (e.g.):** "Hydrogen is not the only compound that has stable or long-lived spinisomers at room temperature (rt) there are many examples: deuterium (Knopp et al., 2003), water (Kravchuk et al., 2011; Vermette et al., 2019), ethylene (Zhivonitko et al., 2013) and methyl groups (Meier et al., 2013). Although some molecules are not symmetric and cannot be extracted at room temperature, they possess long-lived spin states of minutes (Pileio et al., 2008) and hours (Stevanato et al., 2015)."

**Referee comment:** There are a couple of very recent papers describing different parahydrogen generator designs which the authors may wish to cite, doi: 10.1021/acs.analchem.0c03358doi: 10.1016/j.jmr.2020.106869

**Answer:** These papers were not yet published when we finished our manuscript. Nevertheless, we included both generators to our overview table (Table 1).

## 2 RC1: Anonymous Referee

**Referee comment:** "In particular, Page 2, line 46: '0Z axis'? Should it be Z axis?"

**Answer:** As proposed, we changed "0Z axis" to more common "Z axis" in the text

**Referee comment:** "Page 4, line 84: 'don't require much in terms of service' - poor word choice."

**Answer:** We agree and modified the sentence. Actually, the point here is that these setups don't require the supply cryogenes.

**Old text:** "These setups work reliably and don't require much in terms of service (e.g. no liquid cryogenes)."

**New text:** "These setups work reliably and don't require a supply of liquid

cryogens.”

**Referee comment:** ”Page 4, line 90: ’were performed ... - and still are poor word choice.”

**Answer:** We modified the sentence and removed ”still are”.

**Old text:** ”Indeed, much of the initial studies were performed with  $\text{LN}_2$ -based PHGs - and still are (Kiryutin et al., 2017; Meier et al., 2019).”

**New text:** ”Indeed,  $\text{LN}_2$ -based PHGs are still used in many studies (Kiryutin et al., 2017; Meier et al., 2019)”

**Referee comment:** ”Page 4, line 95: ’way beyond’ - poor word choice.”

**Answer:** We agree that it is colloquial and we removed ”way” from the sentence.

**Referee comment:** ”Page 5, line 113: ’Iron (III) oxide’ - should be hydrated iron oxide or  $\text{FeO}(\text{OH})$ .”

**Answer:** We agree and changed it to the more specific name ” $\text{Fe}(\text{OH})\text{O}$ ”.

**New text:** ”About 1.5 ml granular  $\text{Fe}(\text{OH})\text{O}$  (371254-50G, Sigma-Aldrich, St. Louis, U.S.A.) was filled into the coil.”

**Referee comment:** ”Page 8, line 183: should ’norm’ stand for normal pressure and temperature (not standard)? See, for example, [https://www.engineeringtoolbox.com/stp-standard-ntp-normal-air-d\\_772.html](https://www.engineeringtoolbox.com/stp-standard-ntp-normal-air-d_772.html)

**Answer:** We understand that ”stand” is a better choice as an index. Therefore, we substituted ”norm” by ”stand” everywhere, i.e. ” $p_{\text{norm}}$ ” by ” $p_{\text{stand}}$ ”

**Old text:** ”[...] where  $T_{\text{rt}}$  is the temperature of the quantification experiment (here: 22 °C) and ’norm’ stands for standard pressure and temperature values ( $p_{\text{norm}} = 10^5$  pascals = 1.0 bar,  $T_{\text{norm}} = 273.15$  K) (Nic et al., 2009).”

**New text:** ”[...] where  $T_{\text{rt}}$  is the temperature of the quantification experiment (here: 22 °C) and ’stand’ stands for standard pressure and temperature values ( $p_{\text{norm}} = 10^5$  pascals = 1.0 bar,  $T_{\text{stand}} = 273.15$  K) (Nic et al., 2009).”

**Referee comment:** ”Page 10, line 227: ’250 mm internal diameter, 360 mm outer diameter’ - numbers seem too big, please check.”

**Answer:** You are absolutely right! We corrected the unit ”mm” to ” $\mu\text{m}$ ”.

**New text:** ”The only modification was that a hollow optical fibre (Molex, part. num. 106815-0026, 250  $\mu\text{m}$  internal diameter, 360  $\mu\text{m}$  outer diameter) was glued to the end of the PTFE capillaries to reduce magnetic field distur-

tions.”

**Referee comment:** ”Page 11, line 253: ’These collisions’?”

**Answer:** We changed the paragraph in a way, that the choice of word and structure is more appropriate.

**Old text:** ”The flow rate is an important parameter since it affects the collisions of H<sub>2</sub> with the catalyst in the ortho-para conversion unit (Fig. 3, A3). At optimal parameters, IN<sub>2</sub> based PHG can provide  $f_{\text{pH}_2} = 52\%$  (Fig. 2,7b). These collisions are responsible for the fast ortho-para conversion”

**New text:** ”The flow rate is an important parameter since it affects the amount of H<sub>2</sub> collisions with the catalyst in the ortho-para conversion unit (Fig. 3, A3) that enables fast para-ortho-conversion. A IN<sub>2</sub>-based PHG can provide  $f_{\text{pH}_2} = 52\%$  at maximum (Fig. 2,7b).”

**Referee comment:** ”Page 11, line 259: ’ad-hoc’ is used improperly in this sentence.”

**Answer:** We agree that ”ad-hoc” is not the right word in this context. We modified the sentence.

**Old text:** ”This flow rate was fast enough for convenient ad-hoc p<sub>H</sub><sub>2</sub> production.”

**New text:** ”This flow rate was fast enough for a convenient p<sub>H</sub><sub>2</sub> production.”

**Referee comment:** ”Page 12, line 269 and 273: errors and mean values should have the same number of significant figures, i.e., either 51.50(36) or 51.5(4)”

**Answer:** We totally agree and changed all results in the manuscript to the format XX,X ± X,X.

**Old text (e.g.):** ”The average  $f_{\text{pH}_2}$  was found to be  $(51.5 \pm 0.36)\%$ , corresponding to a coefficient of variation (CV) of 0.7% (Fig. 8).”

**New text:** ”The average  $f_{\text{pH}_2}$  was found to be  $(51.5 \pm 0.4)\%$ , corresponding to a coefficient of variation (CV) of 0.7% (Fig. 8).”

### 3 RC2: James Eills

**Referee comment:** Title: "3D-printed" should be removed from the title or clarified as "partially 3D printed" (or similar), as this is misleading in its current form.

**Answer:** We agree. And to avoid this confusion modified the title as follows: New title: "Open-source, partially 3D-printed, high-pressure (50 bar) liquid-nitrogen-cooled parahydrogen generator"

**Referee comment:** Line 40: The authors might choose to also mention long-lived spin isomers in methylrotors, e.g. doi: 10.1021/ja410432f

**Answer:** Thanks for pointing out this paper! We added it to the list.

**Old text:** "Hydrogen is not the only compound that has stable or long-lived spin isomers at room temperature (rt) there are many examples: deuterium (Knopp et al., 2003), water (Mammoli et al., 2015; Meier et al., 2015), ethylene (Zhivonitko et al., 2013), and even naphthalene derivative (Stevanato et al., 2015)."

**New text:** "Hydrogen is not the only compound that has stable or long-lived spinisomers at room temperature (rt) there are many examples: deuterium (Knopp et al., 2003), water (Kravchuk et al., 2011; Vermette et al., 2019), ethylene (Zhivonitko et al., 2013) and methyl groups (Meier et al., 2013)."

**Referee comment:** Line 113: Can the authors make any comment about how well the cotton wool works in preventing iron oxide flow through the system, or state how much was used for effective filtering?

**Answer:** To address this in the text we modified and added one section in the text. Now it is as follows

**New text:** "On both ends of the copper coil, cotton wool was pressed to keep the catalyst in place to protect the rest of the system from contaminations. The compressed wool insets have a length of 20 mm. Wool as a particulate filter was used before in another PHG (Du et al., 2020). During the six months of weekly use of our generator, there was no sign of a moving catalyst."

**Referee comment:** Line 141: It would be helpful to briefly state how inductive and static spark charges are avoided.

**Answer:** That's a good point! In contrast to fluids, gas does not induce charges in pipes. We modified the safety concept and added a sentence to

the discussion.

**Old text:** "iv. Avoidance of inductive and static spark charges"

**New text:** "iv. Avoidance of inductive and static spark charges in the gas lines (due to conductive and groundable pipe material)"

And in discussions: "The risk for static and inductive spark charges in the gas line is low (Department of Labour of New Zealand, 1990). Nevertheless, the gas pipes can be grounded to prevent electrical charges on the parts which are in contact with H<sub>2</sub> gas."

**Referee comment:** Line 265: I'm a little bit confused about the reporting of  $p_{\text{out}}$ , doesn't this value vary in time? Does  $p_{\text{in}}$  describe the gas pressure in the catalyst region? Isn't this the only relevant pressure when considering conversion as a function of flow rate?

**Answer:** We agree on this point.  $p_{\text{out}}$  is varying during filling and now we defined  $p_{\text{target}}$  that is final  $p_{\text{out}}$  value. We changed the whole manuscript accordingly.

**New text:**

Definition:

We refrained from including a flow meter in the setup to keep it simple and robust. Instead, we used the time  $t_{p,V}$  needed to fill a cylinder of a given volume  $V_0$  to a given pressure  $p_{\text{target}}$ ...

And example:

"For the latter, the para-enrichment was found to be constant up to a flow rate of  $f_r = 2$  SLM (for  $p_{\text{in}} = 20$  bar,  $p_{\text{target}} = 10$  bar)."

**Referee comment:** Lines 343-344: But the quantification is performed on a high-field NMR system. Better to say "We have shown that routine pH<sub>2</sub> quality control can be performed with a low-cost benchtop NMR system", or similar.

**Answer:** We agree and modified the sentence.

**Old text:** "Both values are suited for routine pH<sub>2</sub> quality control without a need for an expensive high-field NMR system."

**New text:** "These results indicate, that the routine pH<sub>2</sub> quality control can be performed with a low-cost 1 T benchtop NMR spectrometer."

**Referee comment:** Lines 347-351: I don't understand the value "points loss of fpH<sub>2</sub> per week". A relaxation time is given to describe the exponen-

tial process and this should be sufficient to understand the  $p_{\text{H}_2}$  change each week. Unless I've misunderstood, I suggest simply removing this.

**Answer:** This value is another way to report the lifetime, but it doesn't transfer additional information. We completely removed this paragraph because it seems to be confusing, also to other referees.

**Referee comment:** Line 348: "With 120 days of lifetime, Hövener et al. reported even longer values(2013)." The phrasing of this sentence is a little strange.

**Answer:** We agree and rephrased the paragraph.

**Old text:** "Feng et al. reported a lifetime in aluminium tanks of  $(63.7 \pm 8.3)$  days and about 2 % points loss of  $f_{\text{pH}_2}$  per week (2012). With 120 days of lifetime, Hövener et al. reported even longer values (2013).

**New text:** "The relaxation time constant in aluminium tanks was found to be  $(63.7 \pm 8.3)$  days by Feng et al. (2012) and 120 days by Hövener et al., respectively (2013)."

**Referee comment:** Line 349: It would be helpful to explain why vacuuming the cylinder should lead to a longer  $p_{\text{H}_2}$  lifetime (presumably due to removal of paramagnetic oxygen molecules).

**Answer:** We removed the part related to vacuuming since we did not perform a cleaning procedure with the storage bottles. However, the production protocol features a flushing routine which removes potential air contamination in the cylinder.

**Old text:** "Note, that we did not vacuum our cylinder that can increase the lifetime."

**New text:** "Note, that we did not perform any dedicated cleaning procedure for the  $p_{\text{H}_2}$  storage bottle."

**Referee comment:** Figure 7: It would be informative to include an additional plot showing para-enrichment level as a function of pressure ( $P_{\text{in}}$ ) for a 2 SLM flow rate. This is a suggestion and I do not insist on this for publication.

**Answer:** We did not observe any pressure dependency for the  $p_{\text{in}}$  values we investigated (12 bar, 20 bar, 35 bar, 50 bar) and now it is mentioned in the text:

**New text:** "We also investigated  $f_{\text{pH}_2}$  as a function of the  $p_{\text{in}}$  pressure at a fixed flow rate: a batch was prepared for  $p_{\text{in}}$  equals 12 bar, 20 bar, 35



bar and 50 bar,  $p_{\text{target}} = 10$  bar and a flow rate of 0.9 SLM. No pressure dependency could be observed. The obtained average of  $f_{\text{pH}_2}$  is  $(52.4 \pm 0.8)$  %.”

**Referee comment:** In another interactive comment, Prof. Igor Kopyug has provided two references to other parahydrogen generators described in the literature. I agree that this closely-related work should be cited.

**Answer:** The papers were published after we finished our manuscript. Nevertheless, they provide valuable information to our paper and we included both He-based PHGs into our overview table.

## 4 RC3: Eleonora Cavallari

**Referee comment:** ”I find the title misleading, reading it I thought the authors provided a printable 3D-model of the parahydrogen generator, therefore I suggest to modify it.”

**Answer:** We got the same feedback also from other referees and the new title now reads as follows:

**New title:** ”Open-source, partially 3D-printed, high-pressure (50 bar) liquid-nitrogen-cooled parahydrogen generator”

**Referee comment:** ”The cotton wool filters used to protect the system from catalyst contamination it could be better described.

**Answer:** We agree that the information about the wool was not detailed enough. That’s why we added more information now.

**Old text (e.g.):** ”In both ends of the coil, the cotton wool was pressed to keep the catalyst in place and protect the rest of the system from contaminations.”

**New text:** ”On both ends of the copper coil, cotton wool was pressed to keep the catalyst in place to protect the rest of the system from contaminations. The compressed wool insets have a length of 20 mm. Wool as a particulate filter was used before in another PHG (Du et al., 2020). During the six months of weekly use of our generator, there was no sign of a moving catalyst.”

**Referee comment:** It would be interesting to know the life time if the cylinder had been vacuumed or even washed with  $\text{H}_2/\text{pH}_2$  before being filled

with  $p\text{H}_2$ , in order to verify that the value obtained using this generator is comparable with those reported previously.”

**Answer:** We changed the sentence concerning the vacuuming since we did not investigate it. The life-time of  $p\text{H}_2$  does not depend on PHG but purity of the storage bottle. See production protocol stage 2: Flushing storage bottle. It is the only cleaning procedure that was used.

**Old text:** ”Note, that we did not vacuum our cylinder that can increase the lifetime.”

**New text:** ”Note, that we did not perform any dedicated cleaning procedure for the bottle. Still, the lifetime is sufficiently long to produce  $p\text{H}_2$  once a week.”

**Referee comment:** ”I don’t understand the meaning of ”points loss of  $f_{p\text{H}_2}$ . Is this value related in someway to the polarization obtainable (13) with respect to  $f_{p\text{H}_2} \approx 100\%$ ? The authors should rephrase the sentence to clarify this concept and/or add the formula that defines it.”

**Answer:** Actually, it was another way to present the lifetime. However, it was confusing other referees, too. Therefore, we decided to remove it completely since it does not contain any additional information.

# Open-source, partially 3D-printed, high-pressure (50 bar) liquid-nitrogen-cooled parahydrogen generator

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**Abstract.** The signal of magnetic resonance imaging (MRI) can be enhanced by several orders of magnitude using  
10 hyperpolarization. In comparison to a broadly used Dynamic Nuclear Polarization (DNP) technique that is already used in clinical trials, the parahydrogen ( $p\text{H}_2$ ) based hyperpolarization approaches are less cost-intensive, scalable and offer high throughput. However, a  $p\text{H}_2$  generator is necessary. Available commercial  $p\text{H}_2$  generators are relatively expensive (10,000 – 150,000 €). To facilitate the spread of  $p\text{H}_2$  hyperpolarization studies, here, we provide the blueprints and 3D-models as open-source for a low-cost (<3,000 €) 50 bar liquid nitrogen  $p\text{H}_2$  generator.

## 15 1 Introduction

Nuclear Magnetic Resonance (NMR), as well as Magnetic Resonance Imaging (MRI), are widely used in medical imaging and chemical analysis. Despite the great success of these techniques (Feyter et al., 2018; Lange et al., 2008; Watson et al., 2020), the low signal-to-noise ratio of NMR limits promising applications such as in vivo spectroscopy or imaging nuclei other than  $^1\text{H}$  (Wilferth et al., 2020; Xu et al., 2008). The hyperpolarization of nuclear spins boosts the signal of selected molecules  
20 by orders of magnitude. This way, imaging of the lung or metabolism has become feasible (Beek et al., 2004; Kurhanewicz et al., 2011).

Among techniques, Parahydrogen And Synthesis Allows Dramatically Enhanced Nuclear Alignment (PASADENA) (Bowers and Weitekamp, 1986, 1987; Eisenschmid et al., 1987) has found application from catalysis research to metabolic imaging (Hövener et al., 2018; Kovtunov et al., 2018).

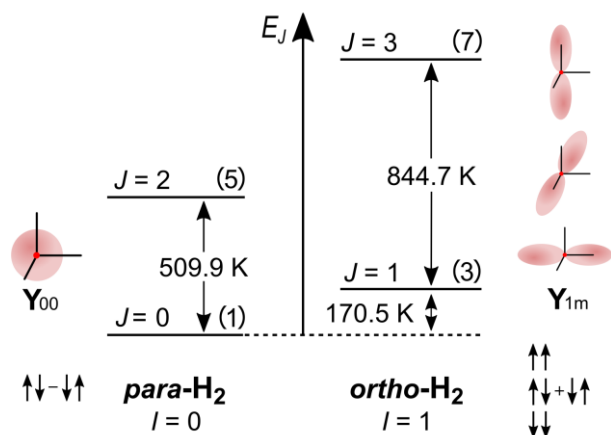
25 The production of parahydrogen ( $p\text{H}_2$ ) is relatively easy:  $\text{H}_2$  gas is flowing through a catalyst at cold temperatures; maximum para-enrichment of almost 100 % is achieved at about 25 K (Gamliel et al., 2010; Jeong et al., 2018; Kiryutin et al., 2017). To reach low temperatures, hence enrich  $p\text{H}_2$ , liquid cryogenics (Buckenmaier et al., 2018; Jeong et al., 2018) or electric cryopumps (Feng et al., 2012) are used. Electronic setups were reported, e.g. for pressures up to 50 bar of  $\approx 100\%$   $p\text{H}_2$  (Hövener et al.,

2013). Liquid nitrogen (LN<sub>2</sub>)-based systems were described, however, often with limited description, low production rate and  
 30 pressure.

Thus, in this contribution, we report a parahydrogen generator (PHG) based on LN<sub>2</sub> that operates at a pressure of up to 50 bar  
 at a cost of less than 3000 €. The setup is easy to replicate as it is fully open-source (Ellermann, 2020b) and all parts are either  
 off-the-shelf, 3D-printed or can be constructed easily. Besides, we introduce an automated *p*H<sub>2</sub> quantification method using a  
 1 T benchtop NMR and an Arduino-based process control.

35 **Background** In 1933 Werner Heisenberg received his Nobel Prize "for the creation of quantum mechanics, the application of  
 which has, inter alia, led to the discovery of the allotropic forms of hydrogen" (NobelPrize.org, 2020). Allotropy is a property  
 of substances to exist in several forms, in the same physical state. Two forms of hydrogen usually are referred to as **nuclear**  
**spinisomers**; they are parahydrogen (*p*H<sub>2</sub>) and orthohydrogen (*o*H<sub>2</sub>). **Hydrogen is not the only compound that has stable or**  
**long-lived spinisomers at room temperature (rt), there are many examples: deuterium (Knopp et al., 2003), water (Kravchuk**  
 40 **et al., 2011; Vermette et al., 2019), ethylene (Zhivonitko et al., 2013) and methyl groups (Meier et al., 2013). Although some**  
**molecules are not symmetric and cannot be extracted at room temperature, they possess long-lived spin states of minutes**  
**(Pileio et al., 2008) and hours (Stevanato et al., 2015).**

The spin of hydrogen nuclei (of protons) is the origin of the two nuclear spinisomer forms of dihydrogen. Protons have spin-  
 45  $\frac{1}{2}$ , hence they are fermions. Fermions are particles that follow the Fermi-Dirac statistics, therefore the sign of the total wave  
 function of H<sub>2</sub> has to change when two nuclei are exchanged. The spin space of two spin- $\frac{1}{2}$  consists of  $(2 \cdot \frac{1}{2} + 1)^2 = 4$  states.  
 They are three symmetric spin states:  $|T_+\rangle = |\alpha\alpha\rangle$ ,  $|T_0\rangle = (|\alpha\beta\rangle + |\beta\alpha\rangle)/\sqrt{2}$ ,  $|T_-\rangle = |\beta\beta\rangle$  and one asymmetric nuclear spin  
 state  $|S\rangle = (|\alpha\beta\rangle - |\beta\alpha\rangle)/\sqrt{2}$  (Fig. 1). Here, conventionally  $|\alpha\rangle$  and  $|\beta\rangle$  states are nuclei spin states with the projection of  
 spin on the **Z** axis  $\frac{1}{2}$  and  $-\frac{1}{2}$ ,  $|T_+\rangle$ ,  $|T_0\rangle$  and  $|T_-\rangle$  are triplet spin states of two spin- $\frac{1}{2}$  with a total spin of 1 and the projection  
 50 on the **Z** axis +1, 0 and -1, and  $|S\rangle$  is a singlet spin state of two spin  $\frac{1}{2}$  with a total spin of 0.



**Figure 1: The rotational energy level diagram for isolated H<sub>2</sub>.** The angular distribution of the two lowest rotational states ( $Y_{00}$  corresponds to  $J = 0$ , and  $Y_{1+1} \pm Y_{1-1}$  and  $Y_{10}$  corresponds to  $J = 1$ ) and spin states of ortho and parahydrogen are indicated. The numbers in parentheses are the degeneracies of the state  $2J + 1$ . The energy of rotation spin states in units of K is equal to  $E_J = J(J + 1)\theta_R$  with  $\theta_R = 87.6$  K (Atkins and De Paula, 2006). The distance between two adjacent energy levels is  $E_{J+1} - E_J = 2(J + 1)\theta_R$ . The figure was inspired by an illustration of I. F. Silvera (1980).

The rotational wave function after nuclei permutation does not change, because of the molecular symmetry, and is only multiplied by  $(-1)^J$ , with  $J$  being the rotational quantum number of the state. Hence, H<sub>2</sub> with a symmetric nuclear spin state (triplet states) can have only an asymmetric rotational state ( $J$  is odd); such H<sub>2</sub> is called  $oH_2$ . And vice versa, H<sub>2</sub> with an asymmetric nuclear spin state (singlet state) can have only symmetric rotation states ( $J$  is even); such H<sub>2</sub> is called  $pH_2$ .

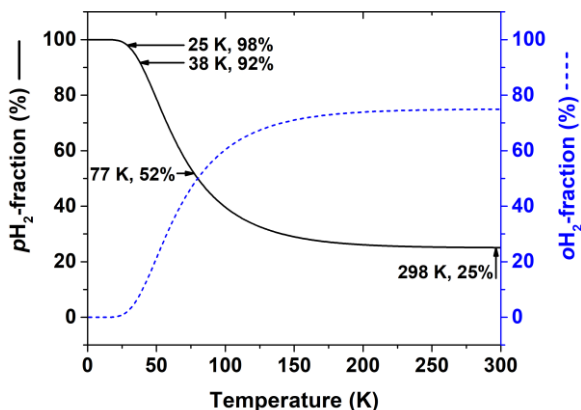
The difference in the energy levels of two ground states of ortho ( $J = 1$ ) and para ( $J = 0$ ) hydrogen is  $E_{J=1} - E_{J=0} = 2\theta_R \cong 175$  K (Fig. 1) (Atkins and De Paula, 2006). Such a big energy gap allows a relatively simple way of spin-isomer enrichment: for H<sub>2</sub> the ground state is  $pH_2$  and its population can be increased by cooling down the gas (Fig. 2) (M. Richardson et al., 2018). The ratio of the number of molecules of  $pH_2$ ,  $n_{pH_2}$ , to  $oH_2$ ,  $n_{oH_2}$ , in thermal equilibrium is given by the Boltzmann distribution of rotational energy levels:

$$\frac{n_{pH_2}}{n_{oH_2}} = \frac{\sum_{J=\text{even} \geq 0} (2J+1) \exp(-J(J+1)\theta_R/T)}{3 \sum_{J=\text{odd} \geq 1} (2J+1) \exp(-J(J+1)\theta_R/T)}. \quad (1)$$

Since only two nuclear spinisomers states of H<sub>2</sub> exist, their fractions can be easily obtained:  $f_{pH_2} = \frac{n_{pH_2}}{n_{pH_2} + n_{oH_2}} = \frac{1}{1 + \frac{n_{oH_2}}{n_{pH_2}}}$  and

$f_{oH_2} = \frac{1}{1 + \frac{n_{pH_2}}{n_{oH_2}}}$ . At room temperatures ( $T \cong 298$  K)  $n_{pH_2} : n_{oH_2}$  is close to 3: 1, at 77 K – the normal boiling point of nitrogen

– the ratio is close to 1: 1, and at 25 K  $f_{pH_2} \cong 98\%$  (Fig. 2).



**Figure 2: Thermal equilibrium fractions of  $pH_2$  and  $oH_2$  as a function of temperature calculated with Eq. 1 and  $J = 6$ .** Four temperatures are marked: (1) 298 K – “room temperature”,  $f_{pH_2} \cong 25\%$ , (2) 77 K – the boiling temperature of liquid nitrogen,  $f_{pH_2} \cong$

52 %, (3) 38 K – medium conversion temperature of Bruker  $p\text{H}_2$  generator,  $f_{p\text{H}_2} \cong 92$  %, (4) 25 K – conversion temperature of high-  
75 pressure PHG,  $f_{p\text{H}_2} \cong 98 \pm 2$  % (Hövenner et al., 2013).

### Technology review

$p\text{H}_2$  fraction,  $f_{p\text{H}_2}$ , of 90 % and above is produced by PHGs with single- or dual-stage cryostats run by Helium compressors. A single-stage cryostat was reported to operate at 36-40 K with a flow rate of 0.2 SLM (Standard Liter per Minute), 10 bar  
80 maximum delivery pressure, and  $f_{p\text{H}_2} \cong 85 - 92$  % (Bruker, Billerica, U.S.A.); dual-stage cryostats operate at temperatures below 25 K where  $f_{p\text{H}_2}$  reaches 100 % (note that the boiling point of  $\text{H}_2$  is 21 K) (Haynes, 2011). All these PHGs were specifically designed with PHIP (ParaHydrogen Induced Polarization) in mind; meaning for a relatively low scale of production and in-lab use (not for the industry). These setups required some on-site assembling and were realized in different designs, e.g. with pulsed injection (Feng et al., 2012) or continuous flow (Hövenner et al., 2013). The continuous flow setup  
85 was reported to operate at a conversion temperature of 25 K, a 4 SLM flow rate, a 50 bar maximum delivery pressure, and an experimentally obtained  $f_{p\text{H}_2} \cong 98 \pm 2$  % (Hövenner et al., 2013).

These setups work reliably and don't require the supply of liquid cryogenes. Disadvantages, however, include high initial investments (40.000 – 150.000 €), some maintenance of the He-compressor and cryostat ( $\approx 10.000$  € every 25.000 h operational time), some site requirements ( $\sim 4$  kW cooling water, appropriate safety precautions) and operational cost in form  
90 of electricity ( $>4$  kW electrical power) (Table 1).

A 100 %  $p\text{H}_2$  enrichment, however, may not always be needed. 50 %  $p\text{H}_2$  fraction provides already 1/3 of the maximum polarization at 1/10 of the costs (or less) (M. Richardson et al., 2018). To achieve  $f_{p\text{H}_2}$  of 50 %, 77 K, the temperature of  $\text{IN}_2$ , is sufficient. Indeed,  $\text{IN}_2$ -based PHGs are still used in many studies (Kiryutin et al., 2017; Meier et al., 2019). The design of such PHGs is generally simple - a catalyst chamber or tube immersed in  $\text{IN}_2$ . But just like cryostat-based PHGs,  $\text{IN}_2$ -based  
95 PHGs are continuously improving. As such, recent advances included a remarkable work, where 20 l  $\text{IN}_2$  were sufficient to provide  $p\text{H}_2$  continuously for 20 days (Jeong et al., 2018).

Interestingly, in various cases it was demonstrated that an increased flow rate and pressure of  $p\text{H}_2$  can boost the signal of PHIP or Signal Amplification By Reversible Exchange (SABRE) (Adams et al., 2009; Rayner and Duckett, 2018) beyond the factor of 3 offered by PHGs with close to  $f_{p\text{H}_2} \cong 100\%$  (Colell et al., 2017; Rayner et al., 2017; Štěpánek et al., 2019; Truong et al.,  
100 2015).

105 **Table 1: Performance comparison of several PHGs:** (1) Bruker PHG 90, (2) dual-stage cryostats (DSC) (Hövenner et al., 2013), (3) a pulsed PHG (Feng et al., 2012), (4) HyperSpin-PHG (Meier et al., 2019), (5) Automated PHG (Birchall et al., 2020), (6) He-dewar PHG (Du et al., 2020), (7) U-shape PHG (Kiryutin et al., 2017), (8) economical PHG (Jeong et al., 2018), (9) glass-trap PHG (Gamliel et al., 2010) and (10) in house designed and built PHG (this work). Given prices include all connectors, cylinders, and 19 % VAT.  $\text{LN}_2$  stands for liquid nitrogen and “cc-He” for closed-cycle He compressor.

Name	Operating temperature (K) [method]	$f_{p\text{H}_2}$ (%)	Initial flow rate (SLM)	Max. pressure (bar)	Price (€)
1 Bruker PHG 90	36-40 [cc-He]	85-92	$\leq 0.2$	10	100,000–150,000
2 DSC (Hövenner et al., 2013)	25 [cc-He]	$98 \pm 2$	4	50	37,000
3 Pulsed PHG (Feng et al., 2012)	15 [cc-He]	98	0.9	20	N.A.
4 HyperSpin-PHG (Meier et al., 2019)	20-77 [cc-He]	N.A. <sup>a</sup>	N.A.	Min. 10	N.A.
5 Automated PHG (Birchall et al., 2020)	40 [cc-He]	$\sim 87$	0.15	33.8	<25,000
6 He-dewar PHG (Du et al., 2020)	30 [He]	$97.3 \pm 1.9$	$\sim 0.3$	4.5	N.A.
7 U-shape PHG (Kiryutin et al., 2017)	77 [ $\text{LN}_2$ ]	$\sim 50$	0.36 <sup>b</sup>	Min. 3	N.A.
8 Economical PHG (Jeong et al., 2018)	77 [ $\text{LN}_2$ ]	$\sim 50$	N.A.	N.A.	N.A.
9 Glass-trap PHG (Gamliel et al., 2010)	77 [ $\text{LN}_2$ ]	$46.3 \pm 1.3$	0.0025 <sup>c</sup>	$\sim 1$	N.A.
10 This work	77 [ $\text{LN}_2$ ]	$51.6 \pm 0.9$	2.0 <sup>d</sup>	50 <sup>e</sup>	2,988 <sup>f</sup>

## 2 Methods

### 2.1 3D design of PHG

110 The principal scheme of a  $\text{LN}_2$ -based complete PHG consists of a  $\text{H}_2$  gas supply, a generator and a  $p\text{H}_2$  storage (Fig. 3). A model of the PHG was designed (Autodesk Inventor 2019, San Rafael, U.S.A.). Aluminium profiles and steel angles (30 mm, Bosch Rexroth, Stuttgart, Germany) were used to construct the chassis. Copper tubes (OD 6 mm, ID 4 mm, rated for 229 bar, R220, Landefeld, Kassel-Industriepark, Germany) and valves (Swagelok, Solon, U.S.A.) were mounted on the chassis using

<sup>a</sup> Depends on choice of coolant

<sup>b</sup> Estimated average flow (3.5 L volume filled to 3 bar in 90 min) calculated by us

<sup>c</sup> Estimated average flow (0.6 L volume filled to 1 bar in 240 min) calculated by us

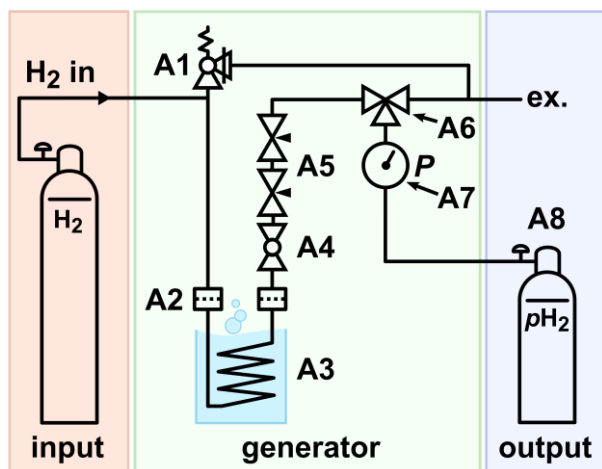
<sup>d</sup> Highest average flow on filling 1 L bottle to 10 bar without sacrificing enrichment

<sup>e</sup> 50 bar  $p\text{H}_2$  delivery was tested. Used parts allow pressure of at least 100 bar (safety margin)

<sup>f</sup> including  $\text{H}_2$ -gas sensor and excluding  $\text{H}_2$  and  $\text{N}_2$  bottles/regulators

3D-printed parts (Ultimaker PLA “Perlweiss” Filament, Ultimaker S5, Ultimaker Cura, Utrecht, Netherlands). A 2 L stainless steel dewar was placed in the chassis (DSS 2000, 2 L, KGW Isotherm, Karlsruhe, Germany). The same copper tubes were used to wind a coil with 5.4 turns and a diameter of 86 mm. About 1.5 ml granular  $\text{Fe}(\text{OH})\text{O}$  (371254-50G, Sigma-Aldrich, St. Louis, U.S.A.) was filled into the coil. On both ends of the copper coil, cotton wool was pressed to keep the catalyst in place to protect the rest of the system from contaminations. The compressed wool insets have a length of 20 mm. Wool as a particulate filter was used before in another PHG (Du et al., 2020). During the six months of weekly use of our generator, there was no sign of a moving catalyst. All fittings, T-pieces, ball-valves, an overpressure-valve, flow regulators, a pressure gauge, and fast connectors (Swagelok, Solon, U.S.A.) were connected with the same copper tube. For the storage of  $p\text{H}_2$ , a 1 L cylinder made from aluminium was used (C1, A6341Q, Luxfer, Nottingham, UK). All parts were chosen to be rated for 100 bar or more to allow for a 100 % safety margin. A list of all parts is given in Appendix A. The models of the PHG, 3D-printing parts and experimental macros (experimental protocols) are available (Ellermann, 2020b).

125



**Figure 3: Schematic view of the PHG.**  $\text{H}_2$  gas is supplied via the inlet e.g. from a 50 L 200 bar cylinder. The gas flows through a filter (A2) into the ortho-para-conversion unit (A3) immersed in  $\text{IN}_2$ , where it is cooling down and thus getting enriched with the  $p\text{H}_2$  component. The parahydrogen-enriched gas exits the ortho-para-conversion unit, warms up and passes another particle filter. The filters reduce the contamination of the setup with catalyst. A ball-valve (A4) is used to start or stop the gas flow. Two needle valves (A5) are used to control the flow rate. A 3-way-valve (A6) allows to fill or drain the storage cylinder. A 100 bar safety valve (A1) is connected to the system to relieve a potential excess of pressure.

## 2.2 Safety concept

A crucial part of a PHG is the development of a safety concept which includes a detailed risk assessment and comprehensive operating manual. The handling of pressurized  $\text{H}_2$  gas entails the risk of pressured gases, forming a potentially explosive mixture with air as well as hydrogen embrittlement (Beeson and Woods, 2003; National Aeronautics and Space Administration, 1997). To reduce these risks, the following safety requirements were set:



## 1. Safety by design

### a. Pressure ratings of parts

- 140 i. All components, in contact with pressurized gas, are rated for minimum 100 bar
- ii. Mechanical pressure gauge
- iii. 100 bar safety valve for overpressure control

### b. Avoidance of formation of explosive H<sub>2</sub>-air-mixture and potential ignition

- 145 i. Reduction of H<sub>2</sub> in the system by minimizing the inner volume of the gas lines
- ii. No electrical components in the system
- iii. Avoidance of temperatures above flame point
- iv. Avoidance of inductive and static spark charges in the gas lines (due to conductive and groundable pipe material)
- v. High H<sub>2</sub> throughput and storage of *p*H<sub>2</sub> in small cylinder leads to a short operating time of PHG

### c. Easy maintenance due to the simple and open design concept

150

## 2. Safety by site and operation

### a. Strong ventilation in the installation site

### b. No public access

### c. Appropriate warning signs

### d. Usage by trained personnel according to manual only

155

### e. Use of safety goggles and safety gloves for the handling of IN<sub>2</sub>

### f. H<sub>2</sub> sensor (for leakage alarm at 50 ppm H<sub>2</sub> level)

### g. Regular inspection and maintenance

## 2.3 Production protocol

160 All *p*H<sub>2</sub> batches were produced in the same manner (the indices in the brackets relate to in Fig. 3):

### *Preparation:*

- Set initial state: Close valve A4, connect the generator with the output via A6 (“fill” position)

- Open and set supply of hydrogen to the appropriate pressure

- Connect the storage bottle A8 to the output

165 - Fill the dewar with IN<sub>2</sub> and close the lid to reduce evaporation

- Wait for 20 min and set the flow with the regulators A5

### *2. Flushing storage bottle:*

- open valve A4 and wait until the pressure gauge shows 3 bar

170 - release gas from the storage cylinder by connecting the storage bottle to the exhaust via A6 (“venting position”)

- repeat the flushing steps three times

### 3. Production and storage of $pH_2$ :

- Set valve A6 to “fill” position

175 - Wait until the gauge shows the desired pressure

- Close valve A4

### 4: Finishing production of $pH_2$ :

- Close storage bottle (bottle valve)

180 - Set valve A6 to “vent” position to reduce pressure in the output line

- Disconnect storage bottle from the output (fast connect adapters keeps line closed)

- Set valve A6 to “close” position

- Close  $H_2$  supply

## 2.4 Quantification

### 185 Flow quantification

We refrained from including a flow meter in the setup to keep it simple and robust. Instead, we used the time  $t^{p,V}$  needed to fill a cylinder of a given volume  $V_0$  to a given pressure  $p_{\text{target}}$  to measure the average flow rate  $f_r$  of the  $pH_2$  production. The pressure  $p_{\text{out}}$  in the outlet of the PHG is increasing during production. To obtain Standard Liters per Minute (SLM) we used the following equation:

$$190 \quad f_r = \frac{V_0}{t^{p,V}} [\text{SLM}] = \frac{p_{\text{out}} V_0 T_{\text{stand}}}{T_{\text{rt}} p_{\text{stand}}} \cdot \frac{1}{t^{p,V}} \quad (2)$$

where  $T_{\text{rt}}$  is the temperature of the quantification experiment (here: 22 °C) and “stand” stands for standard pressure and temperature values ( $p_{\text{stand}} = 10^5$  pascals  $\triangleq$  1.0 bar,  $T_{\text{stand}} = 273.15$  K) (Nič et al., 2009). The measurement of  $f_r$  is performed in a regime where  $p_{\text{out}}$  is linear as a function of time ( $t^{p,V}$ ), hence it coincides with the initial flow rate that is usually reported.

### Gas system

195 A medium-pressure 5 mm NMR tube (522-QPV-8, Wilmad-LabGlass, Vineland, U.S.A.) was used for the  $pH_2$  quantification and a heavy wall 5 mm NMR tube (Wilmad-LabGlass, 522-PV-9) for experiments with Magnetic Field Cycling (MFC). Each of these NMR tubes was equipped with input and output gas lines (1/16” PolyTetraFluoroEthylene capillary (PTFE) with 0.023” inner diameter) by glueing them to the cap. The other end of these tubes was connected to a custom made valve system. The pressure in the system was set by changing the reducers of the respective gases and the back pressure valve in the gas  
200 system (P-785, P-787, Postnova). The inlet gas pressure was regulated to achieve a steady bubbling for the given backpressures of 2.8 bar and 6.9 bar. The valve system is controlled with an Arduino which was linked to the spectrometers software

synchronizing the gas supply, venting of the NMR tube, and data acquisition. Using this gas system we supplied to the NMR tube N<sub>2</sub> (99.999 %, Air Liquide), H<sub>2</sub> (99.999 %, Air Liquide) or *p*H<sub>2</sub>.

### ***p*H<sub>2</sub> quantification protocol**

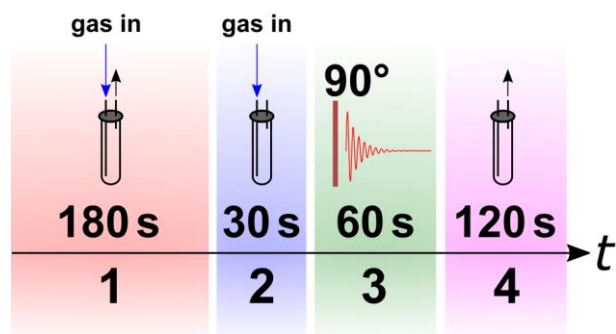
205 The *p*H<sub>2</sub> quantification was performed according to a quantification protocol (schematically shown in Fig. 4).

A NMR tube is placed in a 1 T NMR spectrometer (benchtop, SpinSolve Carbon 43 MHz, Magritek, Aachen, Germany) and not moved during the experiment. To remove air and residual gases from the lines, the setup was flushed with the gas for 3 min at a 5 bar input pressure and a fully open exhaust. Afterwards, the exhaust line was closed and a 30 s delay was allowed to stabilize pressure and flow before the NMR acquisition was started. To ensure the constant pressure in the system, the gas supply was kept open during the NMR measurement. Because the NMR signal was not locked during the experiment, the H<sub>2</sub> resonance was moved to 0 ppm during post-processing for convenience.

210 All NMR spectra of gases were acquired with a standard excitation and acquisition of free induction decay pulse sequence (12.6 μs excitation pulse that corresponds to 90° flipping angle, 20 ms acquisition time, 50 kHz spectral width, 0.5 s repetition time, 100 transients for averaging, SpinSolve Expert v3.54, Magritek, Aachen, Germany). The spectra were subjected to 20 Hz exponential apodization and phase-correction. To remove background signals, a spectrum of N<sub>2</sub> was acquired also and subtracted from the *rt*H<sub>2</sub> (H<sub>2</sub> in thermal equilibrium at room temperature) and *p*H<sub>2</sub> spectra. After that, an automatic baseline correction (MNOVA v14.1.2, Santiago de Compostela, Spain) was applied to the phased spectrum. The spectral lines of *rt*H<sub>2</sub> and *p*H<sub>2</sub> were integrated within the borders of -15 ppm and +15 ppm giving *S*(*rt*H<sub>2</sub>) and *S*(*p*H<sub>2</sub>). Finally the fraction of *p*H<sub>2</sub> *f*<sub>*p*H<sub>2</sub></sub> was calculated:

220 
$$f_{pH_2} = \left(1 - \frac{3}{4} \frac{S(pH_2)}{S(rtH_2)}\right) \cdot 100 \% \quad (3)$$

Here it is taken into account, that only *o*H<sub>2</sub> contributes to the MR signal and *f*<sub>*p*H<sub>2</sub></sub> =  $\frac{1}{4}$  at room temperature (Green et al., 2012).



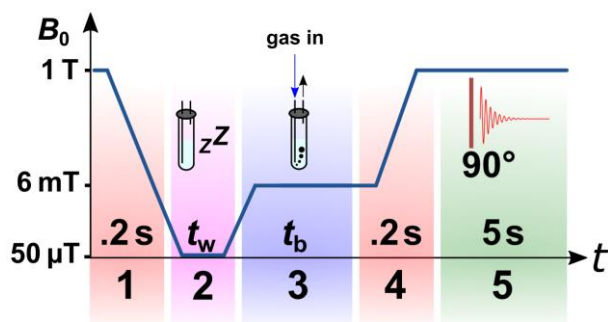
**Figure 4: Scheme of *p*H<sub>2</sub> quantification protocol.** The NMR tube is flushed with N<sub>2</sub>, *p*H<sub>2</sub> or *rt*H<sub>2</sub> gas for 180 s before the exhaust is closed.

225 A rest time of 30 s is allowed for the system to settle down. Finally, the NMR spectra are acquired, before the gas is released.

## 2.5 SABRE experiment

**Sample preparation.** The sample solution contained 3 mmol/L iridium N-heterocyclic carbene complex [Ir(COD)(IMes)Cl], where COD = 1,5-cyclooctadiene, Imes = 1,3-bis(2,4,6-trimethylphenyl) imidazol-2-ylidene (Cowley et al., 2011) and 26 mmol/L nicotinamide (CAS 98-92-0, Sigma-Aldrich) in methanol-d<sub>4</sub> 99.8 % (Deutero GmbH). To activate the catalyst, H<sub>2</sub> was flushed through the sample at 6.9 bar for 5 minutes before the magnetic field cycling experiments begin.

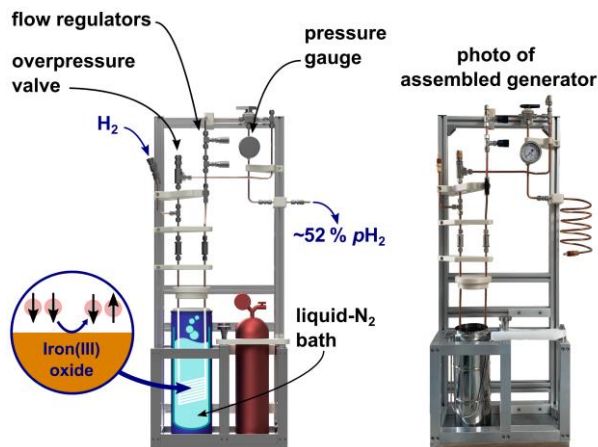
**Magnetic field cycling experiment.** The NMR spectrometer was equipped with an in-house built MFC setup that will be described elsewhere. The shuttling time from the observation point to the sweet spot of the electromagnet was 0.2 seconds. The used electromagnet allowed a magnetic field variation in the range of -20 mT to +20 mT with a magnetic field homogeneity of 0.06 % in 2 cm. The same gas system as described above was used for the MFC SABRE experiments. The only modification was that a hollow optical fibre (Molex, part. num. 106815-0026, 250 μm internal diameter, 360 μm outer diameter) was glued to the end of the PTFE capillaries to reduce magnetic field distortions. All magnetic field-cycling SABRE experiments were carried out according to the protocol in Fig. 5.



**Figure 5: Scheme of <sup>1</sup>H magnetic field cycling SABRE experiment.** Stage 1: shuttling of the sample to the polarization coil. Stage 2: relaxation of the sample at earth's magnetic field for  $t_w = 10$  s. Stage 3: switching on the electromagnet with a magnetic field  $B_p = 6$  mT and starting bubbling with  $p$ H<sub>2</sub> enriched gas at pressure  $P = 6.9$  bar or 2.8 bar for  $t_b = 30$  s. Stage 4: shuttling of the sample to the bore of the NMR spectrometer in 0.2 seconds and turning off the electromagnet. Stage 5: after 90° excitation, acquiring of the <sup>1</sup>H-NMR spectrum.

## 3 Results

### 3.1 PHG design



**Figure 6: a) Rendering of the PHG (left) and a photo of the final build (right).** The design of the PHG is open-source, simple and uses off-the-shelf as well as 3D-printed parts.

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A PHG fulfilling the initial design requirements was successfully constructed (Fig. 6). Most parts were either commercially available, 3D printed or simple to construct on-site. The holders for the bottles and a bottom plate were the sole part prepared by a mechanical workshop. All parts were rated for more than 100 bars and no H<sub>2</sub> leaks were detected at 50 bars of H<sub>2</sub> using a H<sub>2</sub> detector (GasBadge Pro H<sub>2</sub>, Industrial Scientific, Pittsburgh, U.S.A.). Inspection and operation were facilitated by easy access and open construction design. The total cost was below 3,000 € (Appendix A).

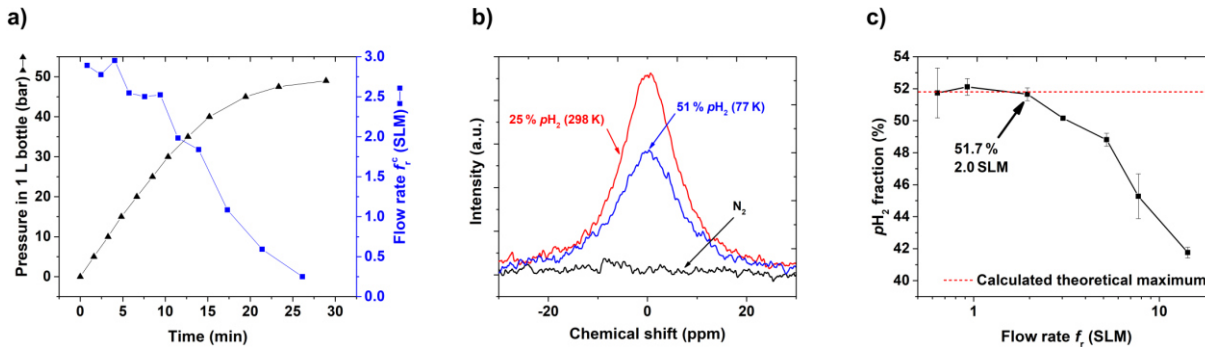
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We deliberately abstained from including a flow meter into the setup to keep the cost low and increase the robustness. Instead, we monitored the pressure  $p_{\text{out}}$  in the storage cylinder and calculated the flow rate (Fig. 7a). The expected increase in pressure and decrease in the flow rate of  $p\text{H}_2$  was observed. The flow rate is an important parameter since it affects the amount of H<sub>2</sub> collisions with the catalyst in the ortho-para conversion unit (Fig. 3, A3) that enables fast para-ortho-conversion. A IN<sub>2</sub> based PHG can provide  $f_{p\text{H}_2} \cong 52\%$  at maximum (Fig. 2,7b). If the flow rate is too fast, the gas will not have enough time to reach the ortho-para thermal equilibrium while passing through the unit. Hence the  $p\text{H}_2$  fraction will be reduced.

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Thus, to find optimal performance conditions of the PHG, we quantified  $f_{p\text{H}_2}$  as a function of the flow rate (Fig. 7c) set by the needle valves (Fig.3, A5). At the given settings of  $p_{\text{in}} = 20$  bar and  $p_{\text{target}} = 10$  bar,  $f_{p\text{H}_2} \approx 51.7\%$  was found for a flow up to  $f_{\text{r}} = 2$  SLM. For larger flow rates, the enrichment dropped significantly. Given this data, and to allow for some variation, we chose a standard operating flow of  $\sim 0.9$  SLM. This flow rate was fast enough for a convenient  $p\text{H}_2$  production. For example, 1 L of 49 bar  $p\text{H}_2$  with  $f_{p\text{H}_2} = (51.7 \pm 0.8)\%$  were produced in 29 min ( $p_{\text{in}} = 49$  bar, initial flow rate of 2.9 SLM, Fig. 7a).

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**Figure 7: PHG operating parameters and NMR spectra:** (a) Pressure  $p_{\text{out}}$  and calculated flow rate  $f_r^c = p'_{\text{out}} \cdot \frac{V_0 T_{\text{stand}}}{T_{\text{rt}} P_{\text{stand}}}$  as a function of time for input pressure  $p_{\text{in}} = 50$  bar and  $V_0 = 1$  L, (b)  $^1\text{H}$  NMR spectra of  $\text{rtH}_2$ ,  $p\text{H}_2$  and  $\text{N}_2$  to quantify  $f_{p\text{H}_2}$ , and (c),  $f_{p\text{H}_2}$  as a function of  $f_r$  (eq. 3). For the latter, the para-enrichment was found to be constant up to a flow rate of  $f_r = 2$  SLM (for  $p_{\text{in}} = 20$  bar,  $p_{\text{target}} = 10$  bar).

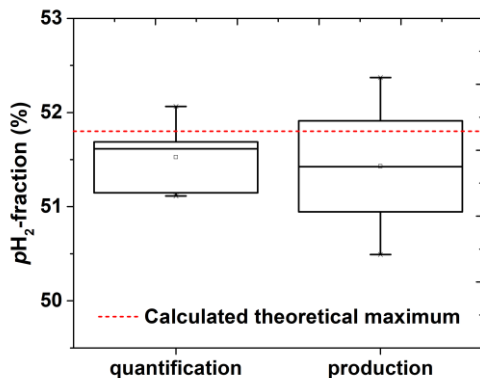
### 3.2 The precision of $p\text{H}_2$ production, quantification and lifetime

To test the reproducibility of the quantification method,  $f_{p\text{H}_2}$  of a single batch was quantified 5 times in a row (including venting, flushing, and filling of the tube). The average  $f_{p\text{H}_2}$  was found to be  $(51.5 \pm 0.4)\%$ , corresponding to a coefficient of variation (CV) of 0.7 % (Fig. 8).

To assess the reproducibility of the entire production process, four  $p\text{H}_2$  batches were produced on different days. An average  $f_{p\text{H}_2}$  of  $(51.6 \pm 0.9)\%$  was observed (CV = 1.7 %) (Fig. 8).

We also investigated  $f_{p\text{H}_2}$  as a function of the  $p_{\text{in}}$  pressure at a fixed flow rate: a batch was prepared for  $p_{\text{in}}$  equals 12 bar, 20 bar, 35 bar and 50 bar,  $p_{\text{target}} = 10$  bar and a flow rate of 0.9 SLM. No pressure dependency could be observed. The obtained average of  $f_{p\text{H}_2}$  is  $(52.4 \pm 0.8)\%$ .

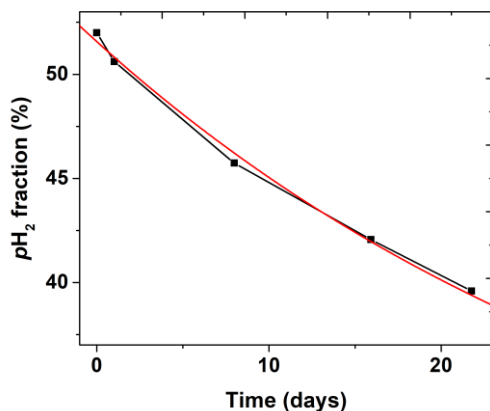
For evaluating the lifetime of  $p\text{H}_2$  in the 2 L cylinder, a 10 bar  $p\text{H}_2$  batch was produced ( $p_{\text{in}} = 20$  bar,  $f_r = 0.9$  SLM). Over 22 days, five samples were taken from the batch and  $f_{p\text{H}_2}$  was quantified. An exponential decay function was fitted to the data and yielded a constant of  $35.5 \pm 1.5$  days (Fig. 9).



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**Figure 8:  $p\text{H}_2$  quantification and production reproducibility chart.** The left boxplot shows the precision of quantification method. The  $p\text{H}_2$  quantification protocol was repeated five times with the same  $p\text{H}_2$  batch. The obtained  $p\text{H}_2$  fraction was  $(51.5 \pm 0.4) \%$  that gives us an impression of quantification precision. The right boxplot shows the reproducibility of the production. The production of  $p\text{H}_2$  and quantification protocols were repeated once on four different days. The obtained  $p\text{H}_2$  fraction here was  $(51.6 \pm 0.9) \%$ ; the error value includes production and quantification errors. PHG parameters of  $p\text{H}_2$  preparation: 20 bar inlet pressure, 10 bar final pressure in the storage cylinder and a 0.9 SLM average flow rate. All errors are given by the standard deviation.

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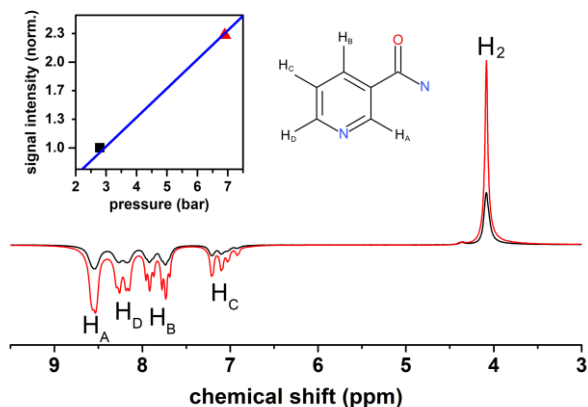
**Figure 9:  $p\text{H}_2$  lifetime in a 2 L aluminium cylinder.** The data is fitted with the exponential decay function:  $A_1 \cdot \exp(-t/\tau) + y_0$  with  $y_0$  fixed to 25,  $A_1 = 26.6 \pm 0.3$  and a resulting relaxation decay time of  $\tau = (35.5 \pm 1.5)$  days.

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### 3.4 Application: $^1\text{H}$ -low-field SABRE at different $p\text{H}_2$ pressures

The presented setup was designed to allow for pressures up to 50 bar. High pressures are beneficial for hyperpolarization because the concentration of  $p\text{H}_2$  in the solution increases with pressure. A low concentration of  $p\text{H}_2$  is often the limiting factor

300 of the hyperpolarization yield (polarization level  $\times$  concentration of polarized species). To demonstrate the effect, we polarized nicotine amide by SABRE and magnetic field-cycling (scheme at Fig. 5) at two different  $p\text{H}_2$  pressures: 2.8 and 6.9 bar (Fig. 10). Strong polarization was observed on  $^1\text{H}$  resonances of nicotine amide and hydrogen in solution and increased at higher pressure. A 2.5-fold increase in pressure yielded a 2.3-fold increase of nicotine amide polarization.



305 **Figure 10:**  $^1\text{H}$ -SABRE spectra of nicotine amide and  $\text{H}_2$  at 6.9 bar and 2.8 bar  $p\text{H}_2$  pressure. (Insert) The signal intensity of nicotine amide vs. pressure with a linear fit (blue line). Nicotine amide structure is added for convenience.

#### 4 Discussion

**Design.** The design of the presented PHG is simple and compact without compromising on performance and safety. The PHG is small and portable (although a heavy bottom plate was added for stability). Since there are no electrical components, it can be placed indoor as well as outdoor and does not require any electrical power supply. Note, electric components can be an ignition source which may lead to an explosion in case of a hydrogen leak.

For the framework, mostly, off-the-shelf parts were used. More complex geometries as e.g. holders for valves or gauges were 3D-printed. They have individual shapes and dimensions and manufacturing in a workshop might lead to high costs and long production lead times. 3D-printing turned out to be a versatile manufacturing method enabling fast prototyping, complex shapes, and low-cost for one-off productions. The design of the PHG and all 3D-models (STL-files, Standard Triangulation Language, and CAD-files, Computer-Aided Design) are provided enabling other groups to adjust the parts to their individual needs (Ellermann, 2020b).

Choosing a small 2 L dewar keeps the design compact and the running costs low since less than 2 L of liquid-nitrogen were required to prepare 1 L of  $p\text{H}_2$  at 50 bar. In combination with a short cooling down time, the setup is perfectly suited for on-site  $p\text{H}_2$  production in a hyperpolarization lab.



**Costs.** The final cost of the PHG incl. the hydrogen sensor is 2,988 € incl. VAT (19 %). If a hydrogen sensor is already available in the lab, the overall costs for the PHG can be pushed down to less than 2,500 € incl. VAT (19 %). A complete set including the PHG, a hydrogen sensor, hydrogen/nitrogen gas as well as a variety of essential tools costs about 3,700 € incl. VAT (19 %).

**Safety.** All parts which are in contact with pressurized gas are rated to at least 100 bar. However, we fixed the operation pressure to 50 bar to get a generous safety margin of 100 %. The risk for static and inductive spark charges in the gas line is low (Department of Labour of New Zealand, 1990). Nevertheless, the gas pipes can be grounded to prevent electrical charges on the parts which are in contact with H<sub>2</sub> gas.

The design of the PHG incorporates a gas path which also enables a safe ventilation of a storage bottle. The design and the choice of parts also consider potential handling errors. For example, the output connectors are closed for pressures up to 17 bar when they are disconnected, i.e. for the case that the storage bottle is disconnected. Thus, no contact between the air in the room and the hydrogen in the PHG occurred. Furthermore, we included a handheld hydrogen sensor that can measure hydrogen concentrations in the parts per million (ppm) regime. The sensor should be always turned on during operation and will indicate potential leakages of H<sub>2</sub> gas.

The setup includes low-temperature cryogenics as liquid nitrogen. To prevent the spilling of liquid nitrogen, the dewar is restrained by the copper tubing inside and the surrounding metal frame. Moreover, a lid covers the liquid nitrogen bath that also reduces the evaporation rate of the cryogen. Since the flask only holds around 2 L of cryogen, the amount of liquid nitrogen that has to be handled is greatly reduced.

Note that PHG should be placed in a non-public lockable enclosure or room with sufficient ventilation and only instructed personnel should operate it.

Our presented safety concept is economical and practical without sacrificing any safety measures. Nevertheless, after setting up the PHG, it should be tested for leakage with inert gas or nitrogen. The part-list also contains a leak detection spray and the H<sub>2</sub> sensor.

**Performance** The enrichment achieved here, e.g.  $f_{p\text{H}_2} = 51.6 \pm 0.9 \%$  for  $p_{\text{in}} = 20$  bar,  $f_r = 0.9$  SLM, was close to the maximum of 51.8 % conditioned by the boiling point of IN<sub>2</sub>, and somewhat higher than reported elsewhere  $f_{p\text{H}_2} = 50 \%$  (Barskiy et al., 2016a, 2016b; Shchepin et al., 2016). Determining the enrichment as a function of flow allowed us to choose an optimal flow of 0.9 SLM for  $p_{\text{in}} = 20$  bar: this rate is e.g. sufficient to fill 1 L bottles to 10 bar in 10 min. The central design criterium of high pressure was successfully met as 1 L of 49 bar  $p\text{H}_2$  were produced in 28 min ( $p_{\text{in}} = 50$  bar). We demonstrated that an increase of  $p\text{H}_2$  pressure can give a proportional increase in polarization (Fig. 10). Obviously, this approach is limited as soon as the hyperpolarization yield is no longer determined by the availability of  $p\text{H}_2$  and cannot provide a polarization above 33% (Korchak et al., 2018).

**$p\text{H}_2$  quantification and production reliability** The automatic quantification process features a CV of 0.7 %; the  $p\text{H}_2$  production and quantification together feature a CV of 1.7 % (Fig. 8). These results indicate, that the routine  $p\text{H}_2$  quality

control can be performed with a low-cost 1 T benchtop NMR spectrometer. The automatization certainly helps to make the process more reliable but is not necessary. Feng et al. used the same quantification approach and reported a precision of 1-3 % for quantification (2012). NMR is a convenient method for  $p\text{H}_2$  quantification, but optical methods may be used, too (Parrott et al., 2019).

360 **The lifetime in aluminium cylinder** The relaxation time constant in aluminium tanks was found to be  $(63.7 \pm 8.3)$  days by Feng et al. (2012) and  $\sim 120$  days by Hövener et al., respectively (2013). We found here a shorter lifetime of  $(35.5 \pm 1.5)$  days in our 2 L aluminium storage bottle. Note, that we did not perform any dedicated cleaning procedure for the  $p\text{H}_2$  storage bottle. Still, the lifetime is sufficiently long to produce  $p\text{H}_2$  once a week.

## 5 Conclusion

365 The presented PHG provides  $f_{p\text{H}_2} \approx 52\%$  at a high pressure of 50 bar reliably ( $\text{CV} = 1.7\%$ ) that provides about 1/3 of the polarization achieved with  $f_{p\text{H}_2} \approx 100\%$ . Because the device provides high-pressure  $p\text{H}_2$ , however, this effect can be partially compensated in the PHIP/SABRE experiment. A new, automated quantification routine at 1 T benchtop NMR proved to be reliable and simple ( $\text{CV} = 0.7\%$ ). The design of PHG is straightforward, easy to manufacture with openly available blueprints and at a cost of less than 3,000 €. The device may facilitate further research on the promising method of parahydrogen-based  
370 hyperpolarization.

## 6 Appendices

**Table A1. Price list of all needed components for high-pressure PHG.** Full list of items required for construction of portable liquid nitrogen parahydrogen generator (without cart) with 6 mm copper connection tubes. Here following format for item names is used: {Name [Company], (Specifications), Article number}. Given prices include 19 % VAT.

No	Name	Amount	Price, incl.VAT (Euro/unit)	Price, incl. VAT (Euro)
<b>Gases and cylinders (148.00 €)</b>				
1	Hydrogen cylinder [Airliquid], (Gas, ALPHAGAZ1, S10-1.8 m3), P0231S10R2A001	1	30.00	30.00
2	Nitrogen cylinder [Airliquid], (Gas, ALPHAGAZ1, S10-1.8 m3), P0271S10R2A001	1	40.00	40.00
3	Aluminium cylinder [Luxfer], (Cylinder, H <sub>2</sub> valve 28,8/21,8 LH), A6341Q	1	78.00	78.00

<b>Regulators, gauges and valves (1578.92 €)</b>				
4	Hydrogen cylinder pressure regulator [AirLiquide], (EUROJET 200/50, DIN 477-1, 6 mm tube outlet), Eurojet_125607	1	279.00	279.00
5	Nitrogen cylinder pressure regulator [Kayser], (in 200 bar, out 0-20 bar, DIN 477-1, 1/4" mm male ISO parallel thread), CK1302	1	128.00	128.00
6	Stainless Steel 1-Piece 40G Series Ball Valve [Swagelok], 0.6 Cv, 6 mm Tube Fitting	1	124.12	124.12
7	Stainless Steel High-Pressure Proportional Relief Valve [Swagelok], 6 mm Tube Fitting	1	253.83	253.83
8	Purple Spring for Proportional Relief Valve [Swagelok], 750 to 1500 psig (51.7 to 103 bar)	1	6.90	6.90
9	Stainless Steel 1-Piece 40G Series 3-Way Ball Valve [Swagelok], 0.90 Cv, 6 mm Tube Fitting	1	191.00	191.00
10	Stainless Steel Low Flow Metering Valve [Swagelok], 6 mm Tube Fitting, Vernier Handle	2	242.52	485.04
11	Gauge up to 100 bar [Swagelok], (6 mm tube fitting)	1	111.03	111.03
<b>Tube and fittings (346.15 €)</b>				
12	Copper tube, CUR6X1R Kupferrohr 6x1 mm, R 220, rolled good, soft, 1m [Landefeld]	5	11.29	56.45
13	Brass Instrumentation Quick Connect Stem with Valve [Swagelok], 0.2 Cv, 6 mm Tube Fitting	2	27.01	54.03
14	Brass Instrumentation Quick Connect Body [Swagelok], 0.2 Cv, 6 mm Bulkhead Tube Fitting	2	54.43	108.86
15	Stainless Steel Tube Fitting [Swagelok], Union, 6 mm Tube OD	1	17.91	17.91
16	Stainless Steel Swagelok Tube Fitting, Union Tee, 6 mm Tube OD	3	36.30	108.90
<b>Rest (Catalyst, H<sub>2</sub> detector, Dewar, ..., 1278.20 €)</b>				
17	Iron(III) oxide [Merck] (catalyst grade, 30-50 mesh), 371254-50G	1	152.00	152.00
18	Hydrogen detector [Industrial Scientific], (GasBadge Pro H <sub>2</sub> , 0–2000 ppm), 18100060-C	1	499.00	499.00
19	Stainless steel liquid nitrogen Dewar flask [Isotherm], (DSS 2000, 2L, h=305, D=114), 2103	1	413.00	413.00

20	Stainless Steel In-Line Particulate Filter [Swagelok], 6 mm Tube Fitting, 90 Micron Pore Size	2	107.10	214.20
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**Gas exhaust line (59.80 €)**

21	Polyamid tube [AS-Drucklufttechnik GmbH], (6x3 mm, 1 m), PA 6X3 BLAU-25	5	1.36	6.80
22	Multiple plug connection [AS-Drucklufttechnik GmbH], (1x8mm, 4x6mm), IQSQ 8060	1	16.00	16.00
23	Reduction plug nipple [AS-Drucklufttechnik GmbH], (8mm to 6mm), IQSG 80H60	1	5.90	5.90
24	Check valve [AS-Drucklufttechnik GmbH], (6mm, 0.2 opening <0.2bar), HIQS 60	1	31.10	31.10

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**Tools (125.00 €)**

25	Clip [AS-Drucklufttechnik GmbH], (0 - 14 mm), SAS 14	1	9.2	9.20
26	Leak Detection Spray, [HM INDUSTRIESERVICE GMBH], 291-1252	1	15.1	15.10
27	Adjustable wrench RF 300 [Proxxon], (max 34 mm), 23994	1	26	26.00
28	Open ended wrench set	1	16.2	16.20
29	Pipe cutter [Landefeld], (3 - 30 mm), 4333097000773	1	57.5	57.50
30	PTFE thread seal tape	1	1.00	1.00

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**Frame parts (132.17 €)**

31	Rexroth profile 2 m each (2x 980 mm, 5x340 mm)	2	38.28	76.56
32	Rexroth <i>Nutenstein</i> M4/M5	14	1.12	15.66
33	Filament for 3D-printer: Ultimaker PLA <i>Perlweiß</i> 2,85 mm 750 g	1	39.95	39.95
34	In-house built metal parts (e.g. from university workshop)	0	0	0
35	Screws M4/M5	0	0	0

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Total price for the basic equipment incl. Hydrogen sensor, excl. VAT 2511.12\*

**Total price for the basic equipment, incl. 19 % VAT 2988.24\***

Total price for the complete set incl. tools and gases, excl. VAT 3082.55\*

Total price for the complete set incl. tools and gases, incl. 19 % VAT 3668.24\*

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\* Overall costs may vary due to change of prices, change of VAT rate, and due to costs which may arise for custom parts (e.g. material or labour costs from the facility's workshop)

## 380 **7 Code availability**

Software for automatic signal recording and gas control will be available from figshare.com (DOI: <http://dx.doi.org/10.6084/m9.figshare.13176830>) (Ellermann, 2020a) and via git (Ellermann, 2020b).

## **8 Data availability**

All experimental data (SpinSolve <sup>1</sup>H NMR spectra of H<sub>2</sub>) and blueprints for the PHG will be available from figshare.com (DOI: <http://dx.doi.org/10.6084/m9.figshare.13176830>) (Ellermann, 2020a). Additionally, all blueprints are also accessible via git (Ellermann, 2020b).

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## **10 Author contribution**

Data curation, investigation, formal analysis, software development (here programming of macros), validation, visualization and writing of the original draft was done by FE. ANP and JBH contributed equally to conceptualization, supervision and reviewing the manuscript.

## 395 **11 Competing interests**

There are no competing interests to declare.

## **12 Disclaimer**

## **13 Financial Support**

We acknowledge support by the Emmy Noether Program “metabolic and molecular MR” (HO 4604/2-2), the research training circle “materials for brain” (GRK 2154/1-2019), DFG - RFBR grant (HO 4604/3-1, № 19-53-12013), the German Federal Ministry of Education and Research (BMBF) within the framework of the e:Med research and funding concept (01ZX1915C), Cluster of Excellence “precision medicine in inflammation” (PMI 1267). Kiel University and the Medical Faculty are

acknowledged for supporting the Molecular Imaging North Competence Center (MOIN CC) as a core facility for imaging in vivo. MOIN CC was founded by a grant from the European Regional Development Fund (ERDF) and the Zukunftsprogramm  
405 Wirtschaft of Schleswig-Holstein (Project no. 122-09-053).

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