CLAIMS

1. A system for determining a physiological condition in at least one analyte using hyperpolarized (HP) nuclear magnetic resonance, the system at least comprising:

a hyperpolarizing (HP) preparation apparatus structure to hyperpolarize a substrate agent;

a sample matrix for containing an analyte,

a microfluidic device provided with at least one measuring chamber structured to accommodate the sample matrix containing the analyte, the microfluidic device being structured to infuse the at least one analyte accommodated in the sample matrix with the hyperpolarized substrate agent;

a NMR apparatus at least comprising a housing defining a target area for accommodating at least the analyte with the hyperpolarized substrate agent, as well as at least one magnet unit and at least one magnetic gradient unit for applying – during use – one or more magnetic field gradients in the target area, and at least one radiofrequency (RF) pulse generation unit for applying one or more sets of RF pulses towards the target area, and a RF receiving unit for acquiring signals, and

a computer processing unit for determining the physiological condition in the analyte by analysing the acquired signals.

2. The system according to claim 1, wherein the hyperpolarizing (HP) preparation apparatus is a hyperpolarizer apparatus, e.g., a dynamic nuclear polarization (DNP) apparatus or a para-hydrogen induced polarization (PHIP) apparatus.

3. The system according to any one or more of the preceding claims, wherein the at least one measuring chamber is in fluid communication with a matrix perfusion supply line for supplying a matrix perfusion medium to the measuring chamber, a hyperpolarized substrate agent supply line for supplying the hyperpolarized substrate agent to the measuring chamber and a chamber exit line, wherein preferably the hyperpolarized substrate supply line is located at a position above a position of the matrix perfusion supply line with respect to a bottom wall of the measuring chamber.

4. The system according to claim 3, wherein the chamber exit line is positioned at a position lower than that of the hyperpolarized substrate supply line and at a position higher than that of the matrix perfusion supply line with respect to the bottom wall of the measuring chamber and wherein preferably the matrix perfusion supply line is positioned at the bottom wall of the measuring chamber.

5. The system according to any one or more of the preceding claims, wherein the microfluidic device comprises a temperature control unit for maintaining at least the analyte with the hyperpolarized substrate agent at body temperature when accommodated in the NMR apparatus.

6. The system according to any one or more of the preceding claims, wherein the computer processing unit is structured to analyse at least the acquired signals using one or more machine learning algorithms.

7. The system according to claim 6, wherein the machine learning algorithm is a computer-implemented artificial neural network, and wherein the computer processing unit furthermore comprises a training unit configured to train the computer-implemented artificial neural network with sequences of signals over time characterizing a training sequence of signals over time with known physiological conditions in an analyte contained in a hyperpolarized analyte agent; and to apply to the computer-implemented artificial neural network sequences of input signals characterizing at least a test sequence of signals over time with an unknown physiological condition in an analyte contained in a hyperpolarized analyte agent; and to analyse each applied test sequence of signals over time to generate a predicted physiological condition in an analyte contained in a hyperpolarized analyte agent for each test sequence of signals over time.

8. A method for determining a physiological condition in an analyte with a hyperpolarized substrate agent using the system according to any one or more of the preceding claims, the method comprising the steps of:
a) providing at least one analyte in a sample matrix;
b) infusing the at least one analyte with a hyperpolarized substrate agent;
c) applying one or more magnetic field gradients to the analyte with the hyperpolarized substrate agent using at least one magnet unit and at least one magnetic gradient unit of the NMR apparatus;
d) applying one or more sets of RF pulses towards the target area using at least

one radiofrequency (RF) pulse generation unit of the NMR apparatus;
e) receiving from a RF receiving unit of the NMR apparatus a sequence of NMR signals over time in response to the one or more sets of RF pulses being applied;
f) generating one or multiple time-frequency representations of the sequence of NMR signals by time-frequency transformation, and
g) analysing the time-frequency representations using one or more machine learning algorithms for determining a physiological condition in the analyte.

9. The method of claim 8, wherein the time-frequency transformation of step f) is selected from the group exemplified by but not limited to Fourier transform.

10. The method of claim 8, wherein the one or more machine learning algorithms are selected from the group exemplified by but not limited to an artificial neural network, a decision tree, a regression model, a k-nearest neighbour model, a partial least squares model, a support vector machine, or an ensemble of the models that are integrated to define an algorithm.

11. The method according to any one of the claims 8-10, wherein the machine learning algorithm is a computer-implemented artificial neural network, and wherein analysing step g) is preceded by the steps of:
i) training the computer-implemented artificial neural network with sequences of NMR signals over time characterizing a training sequence of NMR signals over time with a known physiological condition in an analyte with a hyperpolarized substrate agent;
ii) applying to the computer-implemented artificial neural network sequences of NMR input signals characterizing at least a test sequence of NMR signals over time with an unknown physiological condition in an analyte with a hyperpolarized substrate agent;
iii) analysing each applied test sequence of NMR signals over time to generate a predicted physiological condition in an analyte with a hyperpolarized substrate agent for each test sequence of NMR signals over time.

12. The method according to any one of the claims 8-11, wherein the receiving step b) is preceded by the step of:
iv) hyperpolarizing the substrate agent in a hyperpolarizing (HP) preparation apparatus.

13. The method according to any one of the claims 9-12, wherein after step b), but prior to step c), the method further comprises the step of
b1) maintaining the analyte with the hyperpolarized substrate agent at body

temperature.

14. The system of any of claims 1-7, wherein the sample matrix is formed as a three-dimensional construct comprising open pores and wherein the construct is a gel at least comprising sodium carboxymethyl cellulose.

15. The system according to claim 14, wherein the gel at least comprises 0.5-5% (wt.) sodium carboxymethyl cellulose, in particular 1% (wt.) sodium carboxymethyl cellulose and/or wherein the gel is suitable for cryopreservation.

16. The method of any of claims 8-13, wherein the sample matrix is formed as a three-dimensional construct comprising open pores and wherein the construct is a gel at least comprising sodium carboxymethyl cellulose.

17. A sample matrix for accommodating an analyte for in vitro analysis, the sample matrix formed as a three-dimensional construct comprising open pores and wherein the construct is a gel at least comprising sodium carboxymethyl cellulose.

18. The sample matrix according to claim 17, wherein the gel at least comprises 0.5-5% (wt.) sodium carboxymethyl cellulose.

19. The sample matrix according to claim 17, wherein the gel at least comprises 1% (wt.) sodium carboxymethyl cellulose.

20. The sample matrix according to claim 18 or 19, wherein the gel is suitable for cryopreservation.