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Datasheet for the decision of 2 March 2017

Case Number: T 2353/11 - 3.4.01

Application Number: 04000720.5

Publication Number: 1555538

IPC: G01R33/28, G01R33/46

Language of the proceedings: EN

Title of invention:
Method of fast multidimensional NMR spectroscopy

Applicant:
Bruker BioSpin MRI GmbH

Headword:

Relevant legal provisions:
EPC 1973 Art. 56

Keyword:
Inventive step - (no)

Decisions cited:

Catchword:

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Case Number: T 2353/11 - 3.4.01

D E C I S I O N
of Technical Board of Appeal 3.4.01
of 2 March 2017

Appellant: (Applicant)	Bruker BioSpin MRI GmbH Rudolf-Plank-Strasse 23 76275 Ettlingen (DE)
Representative:	Kohler Schmid Möbus Patentanwälte Partnerschaftsgesellschaft mbB Gropiusplatz 10 70563 Stuttgart (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 21 June 2011 refusing European patent application No. 04000720.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	G. Assi
Members:	T. Zinke
	J. Geschwind

Summary of Facts and Submissions

I. The appeal, filed on 13 August 2011, lies from the decision of the examining division, posted on 21 June 2011, refusing European patent application No. 04 000 720.5, published with publication No. 1 555 538. The statement setting out the grounds of appeal was filed on 20 October 2011.

II. In its decision the examining division refused the application according to a then pending main request due to lack of clarity and of support by the description (Article 84 EPC 1973), contravention of Article 123(2) EPC, lack of an inventive step (Articles 52(1) and 56 EPC 1973) and insufficiency of disclosure (Article 83 EPC 1973 and Rule 42(1)(e) EPC). For a then pending auxiliary request, the examining division held that almost all of the reasons mentioned with regard to the main request equally applied to the auxiliary request.

III. With the statement setting out the grounds of appeal, the appellant (applicant) filed amended claims according to a main request and an auxiliary request and requested:

"*1. das Patent im Umfang der Ansprüche gemäß Hauptantrag aufrecht zu erhalten; 2. hilfsweise das Patent im Umfang der Ansprüche gemäß Hilfsantrag aufrecht zu erhalten*".

The Board understood these requests as meaning that the appellant actually requested that the decision under appeal be set aside and a patent be granted based on a set of claims according to said main request or

auxiliary request (cf. communication of 10 January 2017, point II).

The appellant also provided counter-arguments with regard to the objections raised by the examining division in the decision under appeal.

IV. By summons of 3 November 2016 the appellant was summonsed to oral proceedings due to take place on 2 March 2017. A communication under Article 15(1) RPBA was issued on 10 January 2017 drawing attention to the issues to be discussed during oral proceedings. In particular, the Board raised doubts as to whether the subject-matter of claims 1 of the main and the auxiliary requests, respectively, was based on an inventive step with regard to the disclosure of document D1 (L. Frydman, A. Lupulescu, T. Scherf: *"Principles and Features of Single-Scan Two-Dimensional NMR Spectroscopy"*, JACS 125 (2003), pages 9204-9217) in combination with document D2 (J.H. Ardenkjaer-Larsen, B. Fridlund, A. Gram, G. Hansson, L. Hansson, M.H. Lerche, R. Servin, M. Thaning, K. Golman: *"Increase in signal-to-noise ratio of >10,000 times in liquid-state NMR"*, PNAS 100 (2003),pages 10158-10163).

V. The appellant did not provide any comments to the Board's communication.

VI. With a letter of 14 February 2017, the representative informed the Board that the applicant would not attend the oral proceedings.

VII. The oral proceedings took place as scheduled in the absence of the appellant.

VIII. Claim 1 of the main request reads as follows:

"1. A method of multidimensional NMR (=nuclear magnetic resonance) spectroscopy of a sample, the method comprising the following steps:
employing at least one slice selective magnetic field gradient during an excitation period to assign different magnetic field strengths to a multitude of consecutive spatial regions in the sample,
slice selectively exciting nuclear spins in the consecutive spatial regions at consecutive points in time such that at any subsequent point in time the excited spins in the different spatial regions have experienced different evolution times,
detecting in the direction of the slice selective magnetic field gradient spatially resolved NMR signals from the excited spins during an acquisition period in the presence of a periodically inverted read gradient having the same direction as the slice selective magnetic field gradient generating a gradient echo train and
reconstructing a multidimensional NMR spectrum of the sample from the detected train of echo signals, wherein the different evolution times of the consecutive spatial regions yield the indirect dimension of the multi-dimensional NMR spectrum,
characterised
in that prior to the excitation period the nuclear spins in the consecutive spatial regions are hyperpolarised during hyperpolarisation period,
and that hyperpolarisation is carried out by means of polarisation transfer using dynamic nuclear polarisation (DNP), by means of spin refrigeration technique, or by means of thermodynamic equilibrium at very low temperature and high field."

Claims 2-25 are dependent on claim 1.

IX. Claim 1 of the auxiliary request only differs from claim 1 of the main request in that the last feature reads as follows:

"and that hyperpolarisation is carried out by means of polarisation transfer using dynamic nuclear polarisation (DNP)".

Hence, the alternative hyperpolarisation methods of *"spin refrigeration technique"* and *"thermodynamic equilibrium at very low temperature and high field"* have been deleted.

Claims 2-25 are dependent on claim 1.

Reasons for the Decision

1. The appeal is admissible.

2. Admissibility of requests

The main request and the auxiliary request filed together with the statement setting out the grounds of appeal are admitted into the proceedings according to Art. 12(1)(a) RPBA.

3. Main request

3.1 Notwithstanding the plurality of objections under Article 84 EPC 1973 raised by the examining division against the requests underlying the decision under appeal, the Board is in a position to understand the subject-matter of claim 1 of the main request as

currently on file, so that inventive step can be assessed.

3.2 Article 56 EPC 1973

3.2.1 The appellant pointed out in the grounds of appeal (cf. page 8, section 3, *"D1+D2"*):

"Die vorliegende Erfindung kombiniert zwei an sich bekannte Verfahren, nämlich das aus D1 bekannte 2D-Spektroskopie-Verfahren und spezielle Hyperpolarisationsverfahren (Hauptantrag), insbesondere DNP (Hilfsantrag)."

3.2.2 The Board agrees to this general statement, which is in line with the argumentation in the decision under appeal (cf. section 3.1). In particular, claim 1 of the main request combines NMR spectroscopy features known from document D1 with hyperpolarisation as known from document D2.

3.2.3 According to the well-established problem-solution approach, distinguishing features with regard to a closest prior art document should first be identified.

In the present case, it is undisputed that document D1 can be considered as representing the closest prior art disclosing the features of the preamble of claim 1.

Therefore, the distinguishing features of claim 1 of the main request are the hyperpolarisation features of the characterizing part of claim 1.

3.2.4 The technical effect of these distinguishing features is a better signal-to-noise ratio, as acknowledged in the description of the present application stating that

"It is an object of the present invention to propose a method for fast acquisition of multidimensional NMR spectra of arbitrary, in particular small and/or dilute, samples wherein the multidimensional NMR spectra have an improved signal-to-noise ratio" (cf. page 3, lines 28 to 31 of the application as originally filed).

3.2.5 Document D1 relates to the principles and features of single-scan two-dimensional NMR spectroscopy. It does not claim, however, to be exhaustive. Rather, it explicitly refers to issues to be further addressed, like *"S/N enhancement possibilities"*, for example (cf. page 9216, end of *"Conclusions and Perspectives"*).

3.2.6 Document D2 describes a dissolved-phase DNP-enhanced NMR method leading to improved sensitivity and spectral resolution. As the Title states, an *"Increase of signal-to-noise ratio of >10,000 times in liquid-state NMR"* can be achieved.

3.2.7 In the Board's view, it is reasonable to assume that a person skilled in the art would envisage the possibility of relying on the DNP-enhancing solution according to D2 in order to improve the signal-to-noise ratio of the method disclosed by D1. At any rate, reasons leading to a contrary conclusion are not apparent.

3.2.8 The appellant argued that hyperpolarisation had not been used in 2D NMR spectroscopy before the present invention, since conventional 2D NMR spectroscopy methods were too time consuming (cf. page 9 of the statement of grounds).

However, this allegedly hindering reason is invalidated, at least for the person skilled in the art, in view of document D1 which, for instance, explicitly states that *"The purpose of the present Article is to present an expanded description about the basic principles, potential, and features of this new ultrafast 2D NMR methodology."* (cf. page 9205, paragraph bridging left and right column, underlining added).

3.2.9 Hence, the claimed combination of the teaching of document D1 with hyperpolarisation, as disclosed in document D2, is not based on an inventive step.

3.3 Therefore, the main request is not allowable.

4. Auxiliary request

4.1 Claim 1 of the auxiliary request only differs from claim 1 of the main request in that hyperpolarisation is carried out by means of dynamic nuclear polarisation (DNP).

This method, however, is disclosed by document D2, so that the same reasoning mentioned above for the main request apply to the auxiliary request as well.

Hence, claim 1 of the auxiliary request is not based on an inventive step in view of the combination of documents D1 and D2.

4.2 Therefore, the auxiliary request is not allowable.

5. Due to the assessed lack of inventive step of the main request and the auxiliary request as expressed above, there is no reason to deal with the remaining issues

addressed in the decision under appeal under Articles 84, 83 EPC 1973, Article 123(2) EPC and Rule 42(1)(e) EPC.

6. Right to be heard (Article 113(1) EPC)

The reasons for the present decision are all mentioned in the Board's communication of 10 January 2017. The appellant, however, failed to make any submissions in reply. The Board has no reason to take another view.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

The Registrar: The Chairman:

D. Hampe G. Assi

Decision electronically authenticated