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Datasheet for the decision of 20 January 2025

Case Number: T 0660/22 - 3.5.06

Application Number: 14909103.5

Publication Number: 3239287

IPC: C12M1/34, G01N21/27, G01N33/48, G01N33/483, G06T7/20

Language of the proceedings: EN

Title of invention:
ANALYSIS DEVICE, ANALYSIS METHOD, ANALYSIS PROGRAM, CELL MANUFACTURING METHOD AND CELLS

Applicant:
The University of Tokyo
Nikon Corporation

Headword:
Cell analysis/NIKON

Relevant legal provisions:
EPC Art. 56, 83
RPBA 2020 Art. 11

Keyword:
Inventive step - technicality - measurements (no)
Sufficiency of disclosure - over the whole breadth (no)
Remittal - special reasons for remittal (no)

Decisions cited:
G 0001/19

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 0660/22 - 3.5.06

D E C I S I O N
of Technical Board of Appeal 3.5.06
of 20 January 2025

Appellant: (Applicant 1)	The University of Tokyo 3-1, Hongo 7-chome, Bunkyo-ku, Tokyo 113-8654 (JP)
Appellant: (Applicant 2)	Nikon Corporation 15-3, Konan 2-chome Minato-ku Tokyo 108-6290 (JP)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 3 December 2021 refusing European patent application No. 14909103.5 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	M. Müller
Members:	T. Alecu
	A. Jimenez

Summary of Facts and Submissions

I. The appeal is against the decision of the Examining Division to refuse the application for lack of compliance with Article 83 EPC.

II. The Appellant requested that the decision of the Examining Division be set aside and that a patent be granted on the basis of one of the requests underlying the decision under appeal, i.e. one main request and five auxiliary requests, or on the basis of an auxiliary request labelled auxiliary request "B" filed in reply to the Board's preliminary opinion and to be considered immediately after the main request. The Appellant also requested remittal to the Examining Division on the basis of auxiliary request B.

III. Claim 1 of the main request defines:

An analysis device configured to analyse a series of images obtained by a microscope, the images being images of cells in a vessel to which a stimulus is applied, the analysis device comprising:

a cell region separation unit configured to separate cells in the images and to detect, in the images, a region corresponding to a cell;

a characteristic quantity extraction unit configured to extract from the images characteristic quantities for the cell, these characteristic quantities each being associated with a respective element present in the cell;

a mechanism analysis unit configured to calculate a first correlation and a second correlation, the first correlation being a correlation between a series of a first characteristic quantity extracted by the

characteristic quantity extraction unit and a series of a second characteristic quantity extracted by the characteristic quantity extraction unit, the second correlation being a correlation between a series of a third characteristic quantity extracted by the characteristic quantity extraction unit and a series of a fourth characteristic quantity extracted by the characteristic quantity extraction unit,

each correlation being calculated as a cross-correlation between the respective series, each cross-correlation defining a strength of the correlation between the respective characteristic quantities,

to compare the strength of the calculated first correlation with the strength of the calculated second correlation,

and to construct a model illustrating relationships between predetermined elements of the cell

by joining together selected elements of the predetermined elements, based on predetermined associations between those elements and the respective characteristic quantities and the comparison between the strengths of the first and second correlation.

IV. Claim 1 of auxiliary request B defines:

A cell manufacturing method comprising iteratively, until a predetermined criterion is satisfied, a first process of creating cells and a second process of analysing the created cells

wherein the process of analysing the created cells consists of applying an analysis method comprising:

providing a series of images obtained by a microscope, the images being images of the created cells in a vessel to which a stimulus is applied,

with a cell region separation unit, separating cells in the images and detecting, in the images, a region corresponding to a cell;

with a characteristic quantity extracting unit, extracting from the images characteristic quantities, these characteristic quantities each being associated with a respective element present in the cell with a mechanism analysis unit, calculating a first correlation and a second correlation, the first correlation being a correlation between the a first characteristic quantity extracted by the characteristic quantity extraction unit and a second characteristic quantity extracted by the characteristic quantity extraction unit, the second correlation being a correlation between the a third characteristic quantity extracted by the characteristic quantity extraction unit and a fourth characteristic quantity extracted by the characteristic quantity extraction unit, and to compare strength of the calculated first correlation with strength of the calculated second correlation,

each correlation being calculated as a cross-correlation between the respective series, the cross-correlation defining a strength of the correlation between the respective characteristic quantities; and

with the mechanism analysis unit, constructing a model illustrating relationships between predetermined elements of the cell by joining together selected elements of the predetermined elements, based on predetermined associations between those elements and the respective characteristic quantities and the comparison between the strengths of the first and second correlation, and

wherein the predetermined criterion is that the model representing the correlations between the elements indicates a predetermined relationship.

V. Claim 1 of the first auxiliary request differs from that of the main request by the addition of the following feature:

the predetermined elements being selected from the cell, the nucleus of the cell, organelles, cell matrices, biological materials including cell surface carbohydrate chains, intracellular proteins, peptides, mRNA (nucleic acid), metabolites, reactive oxygen species, protein aggregate, cytoplasm, cell membrane, nuclear membrane, and ions

VI. Claim 1 of the second auxiliary request differs from that of the first auxiliary request by the following amendment:

a cell region separation unit configured to separate cells in the images, to detect, in the images, a region corresponding to a cell, and to identify elements present in the cell from the images;

VII. Claim 1 of the third auxiliary request differs from that of the main request by the following amendment:

each correlation being calculated as a cross-correlation between the respective series, each cross-correlation calculated by comparing sections of the respective series in which an amount of change of the characteristic data is relatively [sic], each cross-correlation defining a strength of the correlation between the respective characteristic quantities

VIII. Claim 1 of the fourth auxiliary request differs from that of the third auxiliary request by adding the feature introduced with the first auxiliary request and

by correcting the amendment of the third auxiliary request to state

an amount of change of the characteristic data is relatively large.

IX. Claim 1 of the fifth auxiliary request differs from that of the fourth auxiliary request by also adding the feature introduced with the second auxiliary request.

X. The main request and the first to fifth auxiliary requests also comprise corresponding analysis method claims.

Reasons for the Decision

The application

1. The application relates to cell analysis. It aims at identifying relationships between "elements configuring mechanisms that control vital phenomena in the cell" (paragraphs 1 to 7). The vital phenomena include, for instance a protein signalling cascade (see paragraph 15), and elements may be cell elements such as the nuclei, but also artificially added elements such as an inhibitor (see paragraphs 20 and 22).

2. For this purpose (see figure 3) images of cells are taken, the images are analysed to detect and segment the cells and their elements, and "*characteristic quantities*" (see e.g. paragraphs 73, 75, 77, 79, 82, 84 etc.) associated with the elements are extracted. Time series of such quantities are formed (paragraph 100) and correlated with one another (paragraphs 101 to 124). The elements and their correlation strengths are

visualised as a graphical model, in which the elements form the nodes and each pair of elements is linked by a line with a thickness representing the correlation strength (paragraphs 125 and 126 and figures 23 to 25).

Main request and first to fifth auxiliary requests (requests underlying the decision under appeal)

The decision under appeal

3. The Examining Division decided that the respective claims 1 of all requests before it did not comply with Article 83 EPC (see points decision 18 to 21).

4. It stated that the claims covered the computation of a "*practically unlimited*" number of characteristic quantities and corresponding first and second correlations (decision, point 13). It also stated that it was not possible to derive, be it from the claims or from the description, which mechanisms were sought and which vital phenomena needed to be observed. The technical purpose of the model and the interpretation of the relationships were lacking (decision, point 15).

4.1 The Examining Division also found that the *"excessive number of alternatives arising would not allow the skilled person to draw a sensible conclusion or inter-pretation for any random combination of alternatives*", that it "*induce[d] inherently* an undue burden *[on] the skilled person to explore the results and come with viable interpretations*", and that a demonstration "*that correlations ma[d]e technical sense*" for all possible alternatives was lacking (decision, points 16 and 17).

4.2 It concluded that the application did not disclose even one way of implementing the invention, and did not

enable the person skilled in the art to carry out the invention over the whole scope of the claim without undue burden (decision, points 14 and 17).

5. In a section titled "*Obiter dicta*", the Examining Division further stated that the extent of disclosure was also relevant to the issue of support under Article 84 EPC, because "*the terms of a claim must be commensurate with, or be justified by, the invention's technical contribution to the art. In the present broadness, in absence of a clear technical effect, it is considered that claim 1 of all requests lacks proper support*" (decision, point 23).

5.1 The Examining Division dismissed the Appellant's argument that the invention was a generic analysis tool capable of analysing images and relationships between elements which should be compared with - and treated like - an oscilloscope, stating: "*The oscilloscope as such is a technical apparatus with a well-defined technical purpose and the choice of the quantities measured depends on the task at hand. In the present case, there is no technical purpose or an associated technical effect because the specific computations and the creation of the model illustrating relationships between predetermined elements of the cell is merely a way of manipulating data. The outcome, in the form of an interpretation of the vital phenomena relating to cells, as broadly stated in the description of the application, is left at the latitude of the user (in this case a biologist)*" (decision, point 25).

The Board's preliminary opinion

6. In its preliminary opinion, the Board agreed with the Appellant that the invention, on the basis of the

claims and of the description, was understood by the skilled person as providing only a "research tool", which did not relate to the investigation of a certain, particular, mechanism or phenomenon. Rather, the description and the claims emphasised the definition of a generic (graph) model based on correlations between time-series of observations. This model was presumably meant to help a researcher in their investigation of any given mechanism or phenomenon.

7. Implementing this research tool caused no difficulty for the skilled person, as the Examining Division also acknowledged. Accordingly, the invention could in fact be carried out by the skilled person as required by Article 83 EPC.

7.1 However, the underlying argument, also developed in the "Obiter dicta" section (see above) - namely that a specific technical purpose or associated technical effect of the invention could not be acknowledged - was still of relevance for allowability of all requests. For no inventive step could be acknowledged if no technical problem was solved (Article 56 EPC) and the Board could not see which technical problem was solved.

8. The extraction of several of the claimed characteristic quantities from an image might correspond to the measurement of physical quantities, but the extraction itself was assumed to be known. The alleged contribution was the creation of the graphical model.

8.1 In this respect, the Examining Division appeared to be correct in stating that the construction of this model was merely a way of manipulating data with no associated technical effect. The correlation data may or may not be useful, in the sense of representing real

interactions or dependencies between elements in the cell. The Board also noted that the data produced by these calculations were, at best, meant to gain scientific knowledge about a natural system, which was insufficient to establish a technical effect according to G 1/19 (see reasons 98).

8.2 The Board noted that a case could be made that the correlation strengths, and the corresponding models, were a form of indirect measurement, and thereby inherently of technical nature (G 1/19, reasons 99). The Board understood the Appellant to have advanced the analogy with an oscilloscope or spectroscope in an attempt to support this view. However, neither the correlation strengths nor the corresponding models appeared to correspond to any specific physical property, so that, already for that reason, their derivation could not be considered as an (indirect) measurement.

Arguments by the Appellant

9. The Appellant argued, with reference inter alia to the description, paragraphs 73, 75, 160, and to figures 16, 17, 24, that the object of the invention was the identification of biochemical pathways in a cell. These were analysed by providing a stimulus to the cell and observing the (time-delayed) responses in the various cell elements. These responses over time were captured in terms of the time series of various quantities (e.g., protein levels, microtubules directionality etc.). The correlations between such time series revealed the signalling mechanism and the "wiring" of the cell, which were visualised in the graphical model. The model was therefore an indirect measurement of

physical reality in the sense of G 1/19, reasons 99, and therefore technical in nature.

10. All the steps involved in the construction of the model provided, respectively preserved, the technical character. The characteristic quantities were associated with cell properties and were extracted from images of cells, and therefore constituted measurements of physical reality. The correlations provided information about the elements in that their strength reflected physical reality, and the same was true for the model.

10.1 Although it was correct to observe that between some quantities there will not be any correlation, establishing this would nonetheless provide information about physical reality.

10.2 The fact that the invention required a high number of computations was not relevant. For instance, using a thermal camera to infer the temperature of a body also involved a high number of computations, but the result was still an indirect measurement of physical reality.

11. The obtained model, i.e. the information on the different biochemical pathways and their strengths, could be used to create cells with different characteristics, e.g. having a membrane with higher permeability for certain substances.

11.1 But irrespective of whether the model was actually used for such a technical purpose, the construction of the model was already technical in nature as an indirect measurement. All technical tools could also be used for non-technical purposes. For instance, some people display a Galileo thermometer only for its aesthetic value, and one may use an oscilloscope merely to

produce aesthetically appealing drawings. The technical character of the model according to the invention did not depend on what use would be made of it, but it was inherent in the model.

The Board's conclusions

12. The Board agrees with some of the Appellant's general arguments. Specifically, the Board agrees that whether or not a method is to be considered an (indirect) measurement method does not depend on the number of calculations involved, and that a method of measurement is of a technical nature regardless of what use is made of its results (G 1/19, reasons 99) and hence also where the results are used for a non-technical purpose. The Board also agrees that the strength of the correlation between physical quantities, even a very small or zero correlation, provides information about physical reality.

13. However, the Board disagrees that all methods of obtaining information about physical reality are measurements within the meaning of G 1/19 (reasons 99).

13.1 The Board considers that any measurement method within that meaning, whether indirect or not, or corresponding device, must be intended to determine a specific and predefined physical quantity. A method of measurement may be called "indirect" if it determines the physical quantity of interest on the basis of the measurement of one or more different physical quantities and a known factual relationship between these quantities.

13.2 Methods comprising the measurement of physical quantities followed by calculations to derive values of interest from the measured values are therefore not

indirect measurement methods, unless the calculations correspond to a known factual relationship between the quantities involved and are used to determine the physical quantity of interest.

13.3 For instance, the calculation of a value which does not represent information about physical reality at all, e.g. the price of a refreshment which rises with the measured temperature, is not part of a measurement method. But even if the calculated value provides information about physical reality, for instance a correlation value between physical quantities, that value itself may or may not correspond to a physical quantity. For illustration, a correlation between substance concentration inside and outside a cell may represent the membrane permeability to that substance, so that correlation value would qualify as a physical quantity. But other correlation values may not correspond to any physical quantity (e.g. the correlation between the shape of a desk and the lighting in a room, as was discussed with the Appellant during the oral proceedings), or that correspondence may not, or not yet, be known.

13.4 Correlations between physical quantities contain information which a scientist can use to investigate, and possibly establish, the relationships between physical quantities. But unless such a factual relationship *is* actually established, these values are "just data, which may be used, for example, to gain scientific knowledge" (G 1/19, reasons 98) and obtaining them is not a measurement within the meaning of G 1/19, reasons 99.

14. It is neither self-evident nor explained in the application that each of the many individual

"characteristic quantities" disclosed (see the references in paragraph 2 above) actually represents a physical quantity of the cell. But at any rate this is not established for the claimed characteristic quantities as they remain entirely undefined.

14.1 Even if it were accepted that these characteristic quantities did represent physical quantities and that extracting them from an image constituted a form of measurement, the correlation values are not set out as measurements of any *specific and predefined* physical phenomenon relating two quantities (e.g. a permeability coefficient). The fact that they convey information reflecting physical reality is not sufficient for them to be qualified as indirect measurements (see point 13 above).

14.2 The same holds for the obtained model, which may or may not represent biochemical pathways and signalling mechanisms.

14.3 The model might assist a scientist in determining actual cell properties, but the claimed device (or method) alone does not achieve this.

15. The Board therefore arrives at the conclusion that neither the device according to claim 1 nor the method according to claim 12 provides indirect measurements in the sense of G 1/19, reasons 99. Also, the claims do not state or imply any technical use. The claimed invention thus does not provide any technical contribution and hence cannot be considered to involve an inventive step in the sense of Article 56 EPC.

Auxiliary request B

16. This request was filed by the Appellant in reply to the preliminary opinion of the Board discussed above. The Appellant argued that the filing was caused by the Board raising a new objection under Article 56 EPC. The amendment carried out in this request introduced an explicit technical purpose of the claimed method, namely the manufacturing of cells, and was therefore an appropriate response to the Board's objection.

17. It is correct that the Board disagreed with the Examining Division's objection under Article 83 EPC and raised an objection under Article 56 EPC instead, but the Board notes that its objection is, in substance, essentially the same as that of the Examining Division. It is still based on the doubt that calculating correlations and constructing a corresponding graphical model has a technical effect.

17.1 The Board accepts, however, that the emphasis and the nuances of its objection were different in that they addressed the question, in view of G 1/19, of whether a technical effect could be established by considering the claimed invention a measurement method or device. It also finds the amendment to be a *bona fide* attempt to respond to this change in emphasis. It therefore admits this request (Article 13(2) RPBA 2020).

Article 83 EPC

18. The sole claim of this request defines

A cell manufacturing method comprising iteratively, until a predetermined criterion is satisfied, a first

process of creating cells and a second process of analysing the created cells,

essentially according to the method according to claim 1 of the main request,

wherein the predetermined criterion is that the model representing the correlations between the elements indicates a predetermined relationship.

19. During the oral proceedings the Board raised the objection under Article 83 EPC that it was insufficiently disclosed how to achieve the objective of creating cells with "a predetermined relationship" between elements.

20. The Appellant acknowledged that the application did not provide disclosure in this regard, but argued that this objective could be obtained by trial and error.

20.1 It was a matter of routine for the person skilled in the art to iteratively modify cells so as to obtain ones with desired characteristics. This may take some time, but the time required to obtain cells with the desired property was not a matter of sufficiency.

20.2 The person skilled in the art could assess the evolution of the graphical model over time in order to understand how to create cells with a good chance of having the desired property.

20.3 But even if the objective could not be attained, this did not matter for sufficiency of disclosure because the claim did not cover a method where the predetermined criterion was not ultimately satisfied.

21. The Board is not convinced. The claim is extremely broad and covers any predetermined criterion. For some such criteria, cells satisfying them will not exist. For others, it will be unclear how to create suitable cells, for instance due to missing insights in biochemical engineering.

21.1 Moreover, the claim does not require that the analysis results of one iteration feed back into the creation of cells in the following iteration. Hence, the claim does not guarantee that during the claimed iteration any progress is made towards the desired objective. The description does not provide any information in this regard either.

21.2 Hence, while the person skilled in the art might be able, based on the common general knowledge, to manufacture cells with certain properties, this is insufficient to show that the claimed invention is disclosed over its full breadth.

22. Also, the Board does not agree that the claim excludes methods in which the "predetermined criterion" is never satisfied (see point 19.3 above).

22.1 The claim clearly states that the method is pursued *until* the predetermined criterion *is* satisfied. If this is not possible, then the method cannot be carried out.

22.2 But even if the interpretation of the Appellant were correct, the claim does not specify, and the description does not disclose, a way of identifying "non-working embodiments" (in the sense of point 21 above), or of terminating the iterative manufacturing

process, for instance for lack of progress. So the conclusion above would not change.

23. The Board concludes that this auxiliary request B does not comply with the provisions of Article 83 EPC.

Remittal for further prosecution

24. The Appellant requested that the Board remit the case to the Examining Division for further prosecution, especially on the basis of auxiliary request B, due to special reasons within the meaning of Article 11 RPBA.

24.1 As special reasons, the Appellant mentioned that the Examining Division might be more specialised and therefore in a better position to appreciate the relevant common general knowledge. In any case, there would be more time to consider all aspects of the case. The Appellant stressed that sufficiency of disclosure with respect to auxiliary request B was only raised and discussed during the oral proceedings before the Board and that remittal would enable a thorough examination of Article 83 EPC.

24.2 The Appellant also suggested that remittal would be beneficial for procedural economy. If the present appeal were dismissed, the Appellant would pursue a divisional application so that the matter would anyway be discussed before the Examining Division. The prosecution of this divisional application could be avoided by remitting the present case.

25. The Board does not see a reason to remit.

25.1 The first, substantive, argument is not convincing. If sufficiency of disclosure with respect to auxiliary

request B was indeed discussed for the first time during the oral proceedings, it was because the appellant introduced this request into the proceedings only after receiving the Board's preliminary opinion. The admittance into the proceedings of a new request does not, in itself, constitute a special reason for remittal. In the present case, the issue of sufficiency of disclosure had already been addressed in the decision under appeal. In particular, the Examining Division expressed itself on the fact that the application did not enable the skilled person to interpret the results produced by the claimed method of analysis (see point 4 above), which interpretation is needed if cells are to be manufactured as claimed in auxiliary request B (see point 21 above). Accordingly, the legal and factual framework remained essentially the same and the Board found it expedient to use the discretion conferred on it under Article 111(1) EPC to examine and rule itself on the auxiliary request B. Also, the Board does not see, nor has the Appellant made efforts to explain, how common general knowledge could lead to the conclusion that the person skilled in the art would be able to create cells satisfying *any* desired criterion, neither in general nor based on the claimed, mostly unspecified models.

25.2 The second argument is also not convincing. The notion of procedural economy relates to the prosecution of one individual patent application or patent and does not extend to hypothetical future proceedings involving other patents or patent applications, not even divisional applications. The Appellant requests the opportunity to continue with the Examining Division the discussion of matters which can be settled on appeal. This is clearly not beneficial for procedural economy in the present case.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

L. Stridde Martin Müller

Decision electronically authenticated