

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 31

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

---

Ex parte WAYNE R. MATSON

---

Appeal No. 1996-2240<sup>1</sup>  
Application 08/105,482

---

ON BRIEF

---

Before WINTERS and WILLIAM F. SMITH, Administrative Patent Judges and  
McKELVEY Senior Administrative Patent Judge.

WINTERS, Administrative Patent Judge.

---

<sup>1</sup> Application for patent filed Aug. 12, 1993. According to appellant, this application is a continuation of application 07/649,676, filed Feb. 1, 1991, which is a continuation-in-part of application 07/643,541, filed Jan. 18, 1991, and a continuation-in-part of application 07/274,505 filed Nov. 21, 1988, now U.S. patent no. 5,104,639, issued, Apr. 14, 1992, which is a divisional of application 06/797,615, filed Nov. 13, 1985, now U.S. patent no. 4,863,873, issued Sep. 5, 1989, which is a continuation-in-part of application 06/670,483, filed Nov. 13, 1984, now abandoned, which is a continuation-in-part of application 06/579,401, filed Feb. 17, 1984, now U.S. patent no. 4,511,659, issued Apr. 16, 1985, which is a continuation-in-part of application 06/472,387 filed Mar. 4, 1983, now abandoned, which is a continuation-in-part of application 06/425,183, filed Sep. 28, 1982, now abandoned, which is a continuation-in-part of application 06/111,917 filed Jan. 14, 1980, now U.S. patent no. 4,404,065, issued Sep. 13, 1983.

Appeal No. 1996-2240  
Application No. 08/105,482

### DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1 through 32, all the claims remaining in the application.

A copy of claims 1, 10, 21, 22 and 27 are representative and are appended to this decision.

The references relied on by the examiner are:

Miyagi et al. (Miyagi)	4,338,811	Jul. 13, 1982
Long et al. (Long)	4,343,767	Aug. 10, 1982
Matson (Matson '873)	4,863,873	Sep. 05, 1989
Matson (Matson '639)	5,104,639	Apr. 14, 1992

W.R. Matson, et al. (Matson 1987), "EC ARRAY SENSOR CONCEPTS AND DTA", Life Sciences, Vol. 41, pgs. 905-908 (1987).

B. Seltzer, et al. (Seltzer), "Fingerprint Pattern Differences in Early- and Late-Onset Primary Degenerative Dementia", Archives of Neurology, Vol. 43, pgs. 665-668 (1988).

C. Banissi-Sabourdy, et al. (Banissi-Sabourdy), "Electroanalytical characterization of Alzheimer's disease and ovine spongiform encephalopathy by repeated cyclic voltammetry at a capillary graphite paste electrode", J. Electroanal. Chem. vol. 343: section 28, Bioelectrochemistry and Bioenergetics, pgs. 127-147 (1992).

The claims stand rejected as follows:

Appeal No. 1996-2240  
Application No. 08/105,482

I. Claims 1 through 32 under 35 U.S.C. § 112, first paragraph, as based on a specification which does not provide adequate written descriptive support for the claimed invention and does not enable any person skilled in the art to make and use the claimed invention.

II. Claims 1 through 32 under 35 U.S.C. § 112, second paragraph, as indefinite.

III. Claims 1 through 32 under 35 U.S.C. § 103 as unpatentable over Miyagi, Long and the admitted state of the prior art.

IV. Claims 1 through 32 under 35 U.S.C. § 103 as unpatentable over Matson 1987 and Seltzer.

V. Claims 1 through 20 under the judicially established doctrine of obviousness-type double patenting (provisional) as unpatentable over claims 1 through 20 of co-pending application serial no. 08/092,543.

VI. Claims 1, 2, 10, 21 through 23 and 27 under the judicially established doctrine of obviousness-type double patenting as unpatentable over claims 1 through 4 of U.S. Patent No. 4,863,873.

VII. Claims 1 through 5, 7 through 10, 21 through 23 and 27 under the judicially established doctrine of obviousness-type double patenting as unpatentable over claims 1, 4 through 8, 10, 12 through 16, 18, 19, 22 and 23 of U.S. Patent No. 5,104,639.

Appeal No. 1996-2240  
Application No. 08/105,482

We affirm rejection V under the doctrine of obviousness-type double patenting (provisional), and reverse rejections I through IV, VI and VII.

### DISCUSSION

#### Enablement and Written Description

The claims on appeal are directed to a method of screening for a given disorder by comparing the electrical signal pattern generated by multiple preselected constituents in a biological sample from a test subject with a data base representative of the frequency distribution of those same constituents in samples from epidemiologically significant populations with, and without, that disorder. Some of the claims are limited to screening for Alzheimer's Disease or Parkinson's Disease.

The rejection of claims 1 through 32 under 35 U.S.C. § 112, first paragraph, is based on the written description and enablement requirements of the statute. On inspection, however, we are unable to identify reasoning which would explain why the specification does not provide adequate written descriptive support for the claimed invention. All of the concerns raised by the examiner appear to have a bearing on whether the claims are based on an enabling disclosure.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. In re Marzocchi, 439 F.2d 220,

Appeal No. 1996-2240  
Application No. 08/105,482

223, 169 USPQ 367, 369 (CCPA 1971). If we can summarize the examiner's principal position, it is that undue experimentation would be required to practice the claimed invention because of the breadth of the claims and the limited number of working examples in the specification ("[it] would require an undue amount of experimentation and follow-up to practice the instant invention for every one of the medical disorders ever known, which is what the instant claims encompass . . . ; there is [are] no working examples of diagnosing diseases other than Alzheimer's Disease . . . and Parkinson's Disease . . . ; there are no working examples in the specification concerning analyzing all of the other body fluids encompassed by the claims . . ."). See the Examiner's Answer, pages 3 through 6.

The examiner is further concerned with the absence of absolute certainty in the specification ("it is not clear how one knows with absolute certainty that the abnormality in the profile arises because of a particular one of the millions of medical disorders presently recognized; . . . there is no conclusive evidence presented for each and every one of the disorders encompassed . . . by the claims"), and with the absence of certain specific information ("[t]he specification fails to identify the method used to classify the samples into control and disease groups"). See the Examiner's Answer, pages 4 and 6.

The claims are indeed broad, and generating a frequency distribution data base for diseases and/or biological samples encompassed by the claims, but not

Appeal No. 1996-2240  
Application No. 08/105,482

demonstrated by working examples, would undoubtedly be time consuming. Nevertheless, the test for undue experimentation is not merely quantitative. As stated in PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996):

[T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation “must not be unduly extensive.” Atlas Powder Co., v. E.I. DuPont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

The Patent and Trademark Office Board of Appeals summarized this point in Ex parte Jackson, 217 USPQ 804, 807 (1982):

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

Moreover, it is well settled that the specification need not disclose what is well known in the art. Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). The examiner has not presented evidence that

those skilled in the art would be unable to identify control and disease populations from which to generate frequency distribution data bases.

We have carefully reviewed the specification, including the working examples, in light of the examiner’s commentary on pages 3 through 6 and 16 through 22 of the Answer.

Appeal No. 1996-2240  
Application No. 08/105,482

We are persuaded that the specification, together with what is well known in the art, provides adequate guidance enabling any person skilled in the art to generate frequency distribution databases and to screen for disorders in addition to those of the working examples; and that the experimentation necessary to practice the full scope of the claimed invention, while considerable, would not be undue. Finally, to the extent that the examiner requires absolute certainty to demonstrate enablement, we note that no legal authority has been cited in support of this requirement. On the contrary, a requirement for absolute certainty would be incompatible with the standard of enablement discussed above.

We hold that the examiner has not set forth a reasonable basis for questioning the enablement of the claims on appeal; accordingly, the rejection of claims 1 through 32 under 35 U.S.C. § 112, first paragraph, is reversed.

#### Indefiniteness

All of the claims on appeal stand rejected as indefinite under 35 U.S.C. § 112, second paragraph. See the Examiner's Answer, pages 7 through 9). To the extent that this rejection concerns the breadth of certain terms (“‘tumors’, ‘carcinomas’ and ‘cardiovascular diseases’ are indefinite since the specification gives no guidance as to what type of tumors, carcinomas and cardiovascular diseases are diagnosed by the instant method” “concerning the ‘living subject organism’ [, c]an this organism be a

Appeal No. 1996-2240  
Application No. 08/105,482

mammal, reptile, amphibian, etc.?” ) we are persuaded that one skilled in the art would have no difficulty in understanding the metes and bounds of these terms, and that “[b]readth is not indefiniteness.” In re Gardner, 427 F.2d 786, 788, 166 USPQ 138, 140 (CCPA 1970). To the extent that this rejection concerns the identity of certain terms (“The ‘P05’ recited in claim 26 is indefinite since this designation represents an individual laboratory-assigned label . . .”), we find that the claims are not indefinite when read in light of the specification.

The rejection of claims 1 through 32 under 35 U.S.C. § 112, second paragraph, is reversed.

#### Obviousness

“The name of the game is the claim,” In re Hiniker Co., 150 F.3d 1362, 1369, 47 USPQ2d 1523, 1529 (CAFC 1998). As always, “[a]nalysis begins with a key legal question -- what is the invention claimed?” since “[c]laim interpretation . . . will normally

control the remainder of the decisional process,” Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1567-68, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert. denied, 481 U.S. 1052 (1987). In its broadest aspect, the claimed screening method comprises comparing the electrical signal pattern generated by multiple preselected constituents in a biological

Appeal No. 1996-2240  
Application No. 08/105,482

sample from a test subject with a data base representative of the frequency distribution of those same constituents in samples from epidemiologically significant populations with, and without, that disorder.

Claims 1 through 32 stand rejected as obvious over Miyagi, Long and the admitted state of the prior art.

Miyagi discloses a method of screening for disease by comparing a two-dimensional pattern diagram representing a test subject's integrated values of chromatographic peaks and retention times, with a reference data base of two-dimensional patterns generated the same way.

Long teaches that liquid chromatography, followed by electrochemical detection and analysis of the effluent, is conventional. At pages 2 and 5 of the specification, appellant indicates that "abnormalities in neurotransmitters and related substances are related to degenerative, neuropsychiatric and behavioral disorders" and that Liquid

Chromatography with Electrochemical Detection (LCEC) is "a common tool for the determination of . . . metabolites in biological fluids."

According to the examiner, "it would have been obvious to one of ordinary skill in

Appeal No. 1996-2240  
Application No. 08/105,482

the art to use a conventional method, such as the electrochemical analysis taught by Applicant and Long et al., for the sample fluid analysis in the process taught by Mivagi [sic, Miyagi] et al. so as to produce patterns which are representative of the electrochemical constituents in a body fluid which Applicant admits are known to be associated with various diseases” and “[i]t would have been obvious to one of ordinary skill in the art to utilize a known process of analysis for detecting known constituents associated with a particular disease if one wanted to diagnose that disease.” See page 13 of the Answer.

Appellant argues essentially that none of the prior art relied on teaches a comparison with a frequency distribution data base (e.g., pages 37 and 39 of the Brief). The examiner addresses this limitation for the first time in responding to appellant’s arguments, asserting that “it would have been obvious to one of ordinary skill in the art to apply conventional mathematical models, such as frequency distribution patterns . . . in order to easily classify disorders since the frequency distribution shows distinct

classifiable differences between biological markers of controls and individuals with the disease.” See pages 27 and 28 of the Answer.

Inasmuch as 35 U.S.C. § 103 requires that obviousness be determined based on the claimed subject matter as a whole, we find that the examiner’s burden of

Appeal No. 1996-2240  
Application No. 08/105,482

establishing a prima facie case of obviousness in the first instance has not been met. Again, in setting forth the rejection in the first instance, the examiner does not address appellant's claim limitation respecting a frequency distribution data base. Nor are we persuaded by the examiner's treatment of this issue in responding to appellant's arguments. It is apparent from the specification that "conventional mathematical models" are not interchangeable in the claimed method. Nevertheless, the examiner has not explained why frequency distribution probability analysis would have been selected over other models, such as linear regression analysis, stepwise regression analysis, or cluster analysis, which cannot successfully distinguish between disease and non-disease populations. See pages 19 through 21 of the Specification.

In our judgment, the reason advanced by the examiner for using frequency distribution analysis in the claimed screening method (" . . . since the frequency distribution shows distinct classifiable differences . . . ") stems from appellant's

description in the specification, and not from the prior art. Accordingly, the rejection of claims 1 through 32 under 35 U.S.C. § 103 as unpatentable over Miyagi, Long and the admitted state of the prior art is reversed.

Appeal No. 1996-2240  
Application No. 08/105,482

Claims 1 through 32 additionally stand rejected as obvious over Matson 1987 and Seltzer.

Matson 1987 teaches that “[c]oulometric electrode series array sensors, coupled with liquid chromatography, provide a route to multiplying the resolving power of conventional [liquid chromatography] by factors of 10 to 50.” The reference suggests that “[t]he use of multiple parameter assays of entire metabolic pathways is potentially a powerful tool for unraveling mechanisms of disorders . . . and classification of neurological diseases” and also describes “various techniques of multiple regression and algorithm construction” as “under investigation.” See the Summary and page 908.

Seltzer discloses frequency distribution analysis of fingerprint patterns (ulner or radical loops, arches and whorls) to distinguish between early- and late-onset primary degenerative dementia.

The examiner argues that “[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to use a frequency distribution as taught by

Seltzer for the classification of neurological disorders by the Matson method because one of skill in the art would have recognized that as taught by Seltzer, the frequency distribution would have shown distinct classifiable differences between biological

markers of controls and individuals with the disease.” See page 15 of the Examiner’s Answer.

Because fingerprint patterns and metabolic profiles are distinct properties or features with no readily apparent connection, we infer that the only nexus between Matson 1987 and Seltzer is that both references are concerned with the classification of neurological disorders. We cannot agree that this alone provides the requisite reason or suggestion to combine the references in the manner proposed by the examiner.<sup>2</sup> A bare assertion that it would have been obvious to analyze any biological sample or parameter using any statistical model previously used to identify the presence of a neurological disorder is insufficient. Further, appellant’s disclosure teaches that statistical models are not interchangeable in the claimed method. The examiner has not explained why frequency distribution probability analysis would have been selected over other models, such as linear regression analysis, stepwise regression analysis, or cluster analysis, which cannot successfully distinguish between disease and non-disease populations. See pages 19 through 21 of the Specification.

Again, we find no reason stemming from the prior art which would have led a person having ordinary skill to the claimed method. In our judgment, the only reason or

---

<sup>2</sup> As stated in Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996) (citation omitted), “It is well-established that before a conclusion of obviousness may be made based on a combination of references, there must have been a reason, suggestion, or motivation to lead an inventor to combine those references.”

Appeal No. 1996-2240  
Application No. 08/105,482

suggestion to combine the references in the manner proposed comes from appellant's specification. Accordingly, the rejection of claims 1 through 32 as obvious over Matson 1987 and Seltzer is reversed.

### Double Patenting

Claims 1 through 20 have been provisionally rejected under the doctrine of obviousness-type double patenting over claims 1 through 20 of copending application serial no. 08/092,543 ('543). The present claims are directed to "screening," while the claims of the '543 application are directed to "diagnosis." The examiner sets forth the obviousness relationship between these sets of claims and provides tenable reasoning. See the Examiner's Answer, the paragraph bridging pages 9 and 10. Appellant does not counter the examiner's reasoning, arguing only that the limitation "to screen said disorders" is not found in claim 1 of the '543 application and therefore "would not be anticipated or rendered obvious by claims 1-20 of the Appellant's copending '543

application." See pages 26 and 27 of the Brief. This general argument does not controvert the examiner's position with a reasonable degree of specificity. Accordingly,

Appeal No. 1996-2240  
Application No. 08/105,482

we affirm the provisional rejection of claims 1 through 20 under the doctrine of obviousness-type double patenting.<sup>3</sup>

Claims 1, 2, 10, 21 through 23 and 27 stand rejected as unpatentable over claims 1 through 4 of U.S. Patent No. 4,863,873, under the doctrine of obviousness-type double patenting; claims 1 through 5, 7 through 10, 21 through 23 and 27 stand rejected as unpatentable over claims 1, 4 through 8, 10, 12 through 16, 18, 19 and 22 through 23 of U.S. Patent No. 5,104,639, on the same ground. None of the patented claims recites comparison with a frequency distribution database, nor is that limitation adequately addressed in either rejection. Like the rejections under 35 U.S.C. § 103, we find no reason stemming from the patented claims which would have led a person having ordinary skill to the claimed method. The rejections of the claims on double patenting grounds over U.S. Patent Nos. 4,863,873 and 5,104,639 are reversed.

---

<sup>3</sup> Claim 21 depends from claim 10, and has been grouped with claims 1 through 20 by appellant (see page 9 of the Brief). It is unclear to this merits panel why it was not included in the provisional obviousness-type double patenting rejection. This issue should be addressed in any further prosecution of this application.

Appeal No. 1996-2240  
Application No. 08/105,482

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

SHERMAN D. WINTERS  
Administrative Patent Judge

WILLIAM F. SMITH  
Administrative Patent Judge

FRED E. McKELVEY  
Senior Administrative Patent Judge

)  
)  
)  
)  
)  
) BOARD OF PATENT  
) APPEALS AND  
)  
) INTERFERENCES  
)  
)  
)

vsh

Appeal No. 1996-2240  
Application No. 08/105,482

Norman P. Soloway  
Hayes, Soloway, Hennessey & Hage  
175 Canal Street  
Manchester, NH 03101

Appendix A  
Claims 1, 10, 21, 22 and 27

1. In a method for screening disorders in a test patient in which biological samples containing electrochemically active molecular constituents from normal, unafflicted control individuals, afflicted, abnormal individuals, and said test patient are electrochemically analyzed to generate electrical signal patterns representative of said electrochemically active molecular constituents of said samples, the improvement which comprises creating a data base of electrical signal patterns representative of the frequency distribution of a plurality of predetermined electrochemically active constituents of biological samples from an epidemiologically significant number of individuals having known categories of disorders and from said unafflicted control individuals, comparing said electrical signal patterns in said data base for conformity to electrical signal patterns representative of the frequency distribution of said predetermined constituents of a fluid sample from said test individual, and diagnosing a disorder in said test patient based upon said comparison.

10. A method according to claim 1, wherein each electrical signal pattern representative of frequency distribution of constituents of said biological samples is generated by the following steps, comprising:

passing each one of said biological samples separately through a liquid chromatographic column for achieving time-space separation of said constituents of said biological sample eluting in the column and an electrochemical detection apparatus for generating electrical signals representative of the electrochemical pattern of said biological sample.

21. A method according to claim 10, wherein said constituents of said biological samples are separated by electrochemical characteristics in said electrochemical detection apparatus.

22. A method for screening disorders in a living subject organism, and including electrochemically analyzing biological samples including

electrochemically active compounds taken from healthy organisms and from organisms suffering from a known disorder, said analysis comprising

passing each one of said biological samples separately through a liquid chromatographic column for achieving time-space separation of said electrochemically active compounds of said sample eluting from said column and an electrochemical detection apparatus to generate electrical signal patterns representative of the frequency distributions of said electrochemically active compounds,

examining said patterns for chaotic or non-linear values,

electrochemically analyzing a biological sample taken from said subject organism to generate electrical signal patterns representative of the frequency distribution of electrochemically active compounds of said sample from said subject organism,

comparing the patterns of said subject's sample for conformity with said chaotic or non-linear values, and

diagnosing a disorder in said subject organism based upon said comparison.

27. A method for screening disorders in a living subject organism, and comprising electrochemically analyzing biological samples including electrochemically active compounds taken from healthy organisms and from organisms suffering from a known type of disorder, said analysis including

passing each one of said biological samples separately through a liquid chromatographic column for achieving time-space separation of said electrochemically active compounds of said samples eluting from said column and an electrochemical detection apparatus to generate an electrical signal pattern representative of said electrochemically active compounds,

Appeal No. 1996-2240  
Application No. 08/105,482

creating a data base of electrical signal patterns representative of frequency distribution of said electrochemically active compounds from said biological samples,

subjecting a biological sample from said subject organism to chromatographic separation and electrochemical analysis to produce electrical signal patterns representative of the frequency distribution of electrochemically active compounds in said subject organism's sample,

comparing the resulting electrical signal patterns of the analysis of said subject organism to said patterns in said data base for conformity therewith, and

diagnosing a disorder in said subject organism based upon said comparison.