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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte NEWTON C. FAWCETT
and JEFFREY A. EVANS

Appeal No. 93-3184
Application 07/392,734¹

ON BRIEF

Before WILLIAM F. SMITH, JOHN D. SMITH and GRON, Administrative Patent Judges.

WILLIAM F. SMITH, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the examiner's refusal to allow claims 16 through 27 which have been twice rejected. As set forth at page 3 of the Supplemental

¹ Application for patent filed August 11, 1989. According to appellants, the application is a continuation-in-part of Application 07/253,906, filed October 6, 1988, now abandoned, which is a continuation of Application 06/780,615, filed September 26, 1985, now abandoned.

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Examiner's Answer, claims 16, 17, 19 through 22 and 24 continue to be rejected while claims 18, 23 and 25 through 27 are now only objected to for depending from a rejected claim. Claims 1 through 15 and 28 through 31 are pending but have been withdrawn from consideration by the examiner under 37 C.F.R. § 1.142(b).

Claim 17 is illustrative of the subject matter on appeal and reads as follows:

17. A device for detecting polynucleotide hybridization comprising:

- (a) a piezoelectric crystal;
- (b) a polynucleotide attached to a surface of said crystal; and
- (c) a means for determining the resonance frequency of said crystal.

The examiner withdrew all prior art rejections in the Supplemental Examiner's Answer. As stated at page 3 of the Supplemental Examiner's Answer, the only remaining rejection is that of claims 16, 17, 19 through 22 and 24 under 35 U.S.C. § 112, first paragraph, as being nonenabled. We reverse.

BACKGROUND

The present invention involves a device for detecting polynucleotide hybridization. As seen from claim 17, the claimed device includes a piezoelectric crystal, a polynucleotide

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attached to a surface of the crystal and a means for determining the resonance frequency of the crystal. The claimed invention takes advantage of the well-known piezoelectric effect, i.e., compression of a piezoelectric crystal generates an electrostatic voltage across the crystal. Since the frequency of a piezoelectric crystal depends upon its effective mass, a change in the mass of the crystal, e.g., by adding material to the surface of the crystal, will change the resonance frequency of the crystal. The measured change of frequency can be correlated to the amount of adsorbed material using known mathematical relationships.

Prior to the present invention, piezoelectric crystals had been used as detectors in analytical chemistry. See Hlavay², of record, which reviews the use of piezoelectric crystals in various analytical methods. Commonly, the piezoelectric crystal is coated with a substance which will interact with the material to be measured. Upon exposure of the coated piezoelectric crystal to the material to be measured, the resulting interaction of the material to be measured with the coated piezoelectric crystal results in the effective mass of the piezoelectric crystal being increased. The resulting change in the resonance

² Hlavay et al. (Hlavay), "Applications of the Piezoelectric Crystal Detector in Analytic Chemistry", Analytical Chemistry, Vol. 49, No. 13, pp. 1890-1898 (November 1977).

frequency of the piezoelectric crystal is measured and the amount of the material to be measured which has been adsorbed by the piezoelectric crystal is determined.

It was also well understood prior to the present invention that a DNA strand will pair with a complementary strand of DNA to form double-stranded DNA and that that phenomenon had led to the technology of determining base sequence homology of DNA through hybridization.

The claimed invention makes use of these known concepts in that a polynucleotide, e.g., DNA, attached to the surface of a piezoelectric crystal will hybridize with its complement when associated with its complement under proper conditions. Such a hybridization will result in the effective mass of the piezoelectric crystal increasing and, consequently, the resonance frequency of the crystal will shift. According to the present invention, the polynucleotide can be bonded either directly or indirectly to the piezoelectric crystal surface. The polynucleotide can be bonded indirectly to the surface of the piezoelectric crystal through use of an appropriate polymer coated on the crystal surface to which the polynucleotide is subsequently attached or the polynucleotide may be attached to the piezoelectric crystal surface via a so-called linker compound.

DISCUSSION

As stated at page 3 of the Examiner's Answer, it is the examiner's position that the claims must be limited to "the detection of hybridization between polynucleotide sequences via the use of a coated, AT cut, 9 MHz quartz crystal, wherein a polynucleotide sequence is attached to said quartz crystal through the use of a linker compound." No further explanation of the rejection is given in the statement of the rejection.

The examiner's decision concerning which claims are subject to this rejection and which claims are free of this rejection is not logical. For example, claim 18, which is not rejected, further limits claim 17 only by requiring that a substantial portion of the attached polynucleotide is attached to an electrode material on at least a portion of the crystal. The crystal material of claim 18 is not limited as required by the examiner, i.e., this claim is not limited to an AT cut, 9 MHz quartz crystal. Why claim 18 is not included in the rejection is not apparent from this record. Nor do the other claims not subject to this rejection, claims 23 and 25 through 27, contain the limitations which the examiner has determined must be present in order for them to be considered enabled.

The lack of a complete explication of the rejection and the illogical grouping of the claims in this rejection are

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indications that the examiner has not properly considered the issue of enablement. While the examiner attempts to further explain the basis of the rejection in responding to appellants' arguments, that further explanation amounts to no more than unsupported conclusions regarding the state of the prior art and the level of skill in this art, and is not consistent with appellants' disclosure of the claimed invention.

For example, at page 6 of the Examiner's Answer, the examiner makes reference to the use of a polymer as the "linker." As disclosed and claimed, the present invention involves the "attachment" of the polynucleotide to the surface of the piezoelectric crystal in a broad manner. That "attachment" can be accomplished through the use of a polymer (specification, page 8, lines 21 through 36) or a "linking reagent" which can react with the polymer (specification, page 9, line 33 through page 10, line 4). Thus, contrary to the examiner's treatment of the subject matter, appellants distinguish between a polymer and a linker as means for attaching the polynucleotide to the surface of the piezoelectric crystal.

As set forth above, the examiner's requirement that the claims be limited to an AT cut, 9 MHz quartz crystal wherein the polynucleotide sequence is attached to the crystal through the use of a linker compound has not been well explained. Appellants

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disclose and the prior art, e.g., Hlavay, confirms that there are many different piezoelectric crystals and that AT cut, 9 MHz quartz crystals are the most commonly used. The examiner has not satisfactorily established that one of ordinary skill in the art would have any difficulty in constructing and using a device according to the claims on appeal using other piezoelectric crystals.

Furthermore, the examiner's requirement that the polynucleotide sequence be attached to the piezoelectric crystal through the use of a linker compound does not take into account the alternative methods of attachment disclosed, e.g., the use of an appropriate polymer coating. The examiner has not begun to properly explain in the first instance why one of ordinary skill in the art would not have been able to construct and use the claimed device using the disclosed polymers as the needed means to attach the polynucleotide to the surface of the piezoelectric crystal.

Absent a more complete, logical, fact based explanation of the rejection, we do not find that the examiner has properly established that claims 16, 17, 19 through 22 and 24 are

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nonenabled. The rejection under 35 U.S.C. § 112, first paragraph, is reversed.

NEW GROUND OF REJECTION UNDER 37 C.F.R. § 1.196(b)

Under the authority of 37 C.F.R. § 1.196(b), we make the following new ground of rejection.

Claims 16 through 21 are rejected under § 102(b) as anticipated by Oliveira³, or alternatively under 35 U.S.C. § 103 as unpatentable over this reference.

Oliveira describes a device which comprises a piezoelectric crystal, an antigen attached to a surface of the crystal and a means for determining the resonance frequency of the crystal. The examiner recognized this and applied Oliveira as prior art under 35 U.S.C. § 103, explaining that Oliveira discloses the same device except for having a polynucleotide attached to the surface of the crystal. However, as recognized by appellants at page 10 of the Appeal Brief, Oliveira's definition of an antigen includes nucleic acids, i.e., polynucleotides. See column 5, lines 13 through 16 of Oliveira. Thus, when it is considered that the antigen of Oliveira may be a

³ U.S. Patent No. 4,242,096 issued December 30, 1980 to Oliveira et al. (Oliveira), copy of record.

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polynucleotide, Oliveira specifically describes a device encompassed by claims 16 and 17. Since Oliveira also states that the piezoelectric crystal of that invention may be a quartz crystal, the device of claim 20 is also described by this reference.

In regard to claims 18 and 19, we point to column 4, lines 20 through 23 and 60 through 65 of Oliveira where it is stated that the antigen may be immobilized either directly upon the electrode of the piezoelectric crystal or indirectly on a polymeric primer coat applied to the electrode. In regard to the electrode material specified by claim 21 on appeal, see the paragraph bridging columns 3 and 4 of Oliveira.

In making this anticipation rejection, we note that the intended use of the device for detecting polynucleotide hybridization does not provide any further structure to the device. The claimed device does not differ from that described in Oliveira.

Alternatively, if it is subsequently considered or determined that Oliveira does not describe the claimed device with the specificity needed in order for the reference to be called anticipatory due to the reference describing multiple

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embodiments, see, e.g., In re Arkley, 455 F.2d 586, 172 USPQ 524 (CCPA 1972), we hold that the reference clearly suggests the construction of a device in accordance with these claims. Therefore, the subject matter of these claims would have been obvious to one of ordinary skill in the art.

OTHER ISSUES

Claims 22 through 27 are free of rejection. However, it does not appear from this record that the examiner's consideration of the patent application has included the prior art knowledge regarding materials which can serve to bind polynucleotides to the surface of piezoelectric crystals. While Oliveira specifically discloses that a polymeric primer coat may be used for this purpose, Oliveira does not disclose the specific polymers required by claims 23 through 26. Nor does Oliveira specifically describe attaching a polynucleotide to a solid surface through use of a linker compound such as organic compounds containing an azido group as required by claims 22 and 27.

Upon return of the application, the examiner should see to it that all aspects of the claimed invention have been properly considered and searched before taking further action in the application.

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The second issue which the examiner and the appellants should consider concerns the Bioprocessing Technology reference of record⁴. This reference states that a company has developed technology based on the sensitivity of piezoelectric crystals to minute changes in surface mass caused by certain adsorption of analyte molecules. The disclosed probe is stated to employ a variety of agents including DNA. The reference also sets forth details of how to obtain further information on this technology.

The DNA probe described in this reference appears to be relevant in determining the patentability of the claims on appeal. The examiner and appellants should make reasonable inquiry to determine the prior art status of the technology referenced in this publication.

Any request for reconsideration or modification of this decision by the Board of Patent Appeals and Interferences based upon the same record must be filed within one month from the date of the decision (37 C.F.R. § 1.197). Should appellants elect to have further prosecution before the examiner in response to the new rejection under 37 C.F.R. § 1.196(b) by way of amendment or showing of facts, or both, not previously of record, a shortened statutory period for making such response is hereby set to expire two months from the date of this decision.

⁴ Bioprocessing Technology, Vol. 7, No. 3 (March 1985).

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