

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte ANTHONY J. BROOKES

Appeal No. 2006-0258
Application No. 09/755,747

ON BRIEF

Before ADAMS, MILLS, and GREEN, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-5, 7-18, 20-31, 33-44, 46-52, and 67-76, which are all the claims pending in the application.

Claim 1 is illustrative of the subject matter on appeal and is reproduced below:

1. A method of detecting DNA variation by monitoring the formation or dissociation of a complex consisting of:
 - (a) a single DNA strand of a double stranded DNA of at least 40 base pairs containing the locus of a variation, wherein said single DNA strand is within a monolayer of single DNA strands which are bound to a solid surface,
 - (b) an oligonucleotide or DNA analogue probe specific for one allele of the variation and capable of hybridizing to the single strand (a) to form a DNA duplex,

- (c) an intercalating dye specific for the DNA duplex structure of (a) plus (b) which forms a complex with the duplex and reacts uniquely when interacting within the DNA duplex, which method comprises:
- (1) steadily and progressively adjusting temperature at a rate of between 0.01 to 1°C per second,
 - (2) continually measuring an output signal indicative of interaction of the dye with duplex formed from the strand (a) and probe (b), and
 - (3) recording the temperature at which a change in reaction output signal occurs which is attributable to formation or dissociation of the complex and is thereby correlated with the strength with which the probe (b) has hybridized to the single strand (a).

The references relied upon by the examiner are:

Konrad	5,789,167	Aug. 4, 1998
Heller, et al. (Heller)	6,048,690	Apr. 11, 2000
Wittwer, et al. (Wittwer)	6,174,670	Jan. 16, 2001

Stimpson et al. (Stimpson), "Real-time detection of DNA hybridization and melting on oligonucleotide arrays by using optical wave guides," Proc. Natl. Acad. Sci., Vol. 92, pp. 6379-6383 (1995)

Jordan et al. (Jordan), "Surface Plasmon Resonance Imaging Measurements of DNA Hybridization Adsorption and Streptavidin/DNA Multilayer Formation at chemically Modified Gold Surfaces," Anal. Chem., Vol. 69, pp. 4939-4947 (1997)

GROUNDINGS OF REJECTION

Claims 1-5, 7-18, 20-31, 33-44, 46-52, and 67-76 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Claims 1-5, 8, 10-18, 21, 23-31, 34, 36-44, 47, 49-52, 67-71, 73, 74, and 76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson and Wittwer.

Claims 1-5, 7, 8, 10-18, 20, 21, 23-31, 33, 34, 36-44, 46, 47, 49-52, and 67-76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer, and Heller.

Claims 1-6, 8-19, 21-32, 34-45, 47-52, 67-71, 73, 74, and 76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer and Konrad.

We reverse.

DISCUSSION

New Matter:

Claims 1-5, 7-18, 20-31, 33-44, 46-52, and 67-76 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. More specifically, the examiner finds appellant's September 3, 2003 amendment of the claims to include the term "monolayer" introduces new matter into the specification. According to the examiner (Answer, page 4, emphasis added),

[t]he amendment to include the term "monolayer" is new matter. The specification of the instant application was word[]searched, both by an optical character recognition of the specification in the computer version of the application as well as by a word search of the published application. The word "monolayer" as well as the broader term "layer" were both searched (including plurals) and no basis was found for these terms. The response confines itself to the bare statement that "no new matter has been added by the amendments or new claims (see page 14 of response)" but no specific support for the term "monolayer" is identified in the response. Therefore, in the absence of any identified support for the term, the claims are rejected as containing new matter.

From the foregoing, it is clear that the basis for the examiner's rejection is that the term "monolayer" does not appear in appellant's specification. We note, however, that it is not necessary for the specification to describe the claimed invention ipsissimis verbis; all that is required is that it reasonably convey to those skilled in the art that, as of the filing date sought, the inventor was in possession of the claimed invention. Union Oil of California v. Atlantic Richfield Co., 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000); Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989); In re Edwards, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978).

So the question before us is not whether appellant's specification contains the word "monolayer," rather the question is whether a person of ordinary skill in the art¹ would have recognized from appellant's specification that appellant was in possession of a "monolayer of single DNA strands which are bound to a solid surface," as required by appellant's claimed invention. The specification need not always spell out every detail; only enough "to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation." LizardTech Inc., v. Earth Resource Mapping, Inc., 424 F.3d 1336, 1344-45, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005).

¹ We remind the examiner that written description is determined from the perspective of what the specification conveys to one skilled in the art. In re GPAC Inc., 57 F.3d 1573, 1579, 35 USPQ2d 1116, 1121 (Fed. Cir. 1995); Vas-Cath Inc. v. Mahurkar, 935 F.2d at 1563-64. 19 USPQ2d at 1117.

For his part, appellant directs attention (Brief, page 9), to page 11, lines 9 and 10 of his specification, which discloses “[t]he current binding surface format used is a 96 well microtitre plate that has been coated with streptavidin (available from various manufacturers).” According to appellant (Brief, page 10, emphasis removed), “these types of plates are a generic staple of commerce,” which “can be obtained from a slew of commercial suppliers.” The examiner finds (Answer, page 12), however, that claim 1 “has no limitation to the specific plate used but [instead, it] is broadly drawn to any solid surface.” According to the examiner (Answer, page 13), “[t]he current claims encompass beads, nitrocellulose paper, nylon, slides, silicon chips and any other support used in the art.”

While we agree with the examiner’s interpretation of the scope of claim 1, the question before us on appeal is not an issue of claim scope, e.g., the number of different solid surfaces that fall within the scope of appellant’s claim. To the contrary, the question before us on this appeal is whether appellant’s specification provides written descriptive support for a solid surface to which a monolayer of single DNA strands are bound.² Stated differently, is a 96 well microtitre plate that has been coated with streptavidin, or more specifically, whether the Boehringer-Mannheim streptavidin-coated plate³ set forth in

² See e.g., (Answer, page 12), “[t]he question that now arises is whether this statement [at page 11, lines 9-10 of appellants’ specification] is sufficient to disclose a device with an inherent property of having a ‘monolayer’.”

³ Appellants assert (Brief, page 9), “[t]he specification, at page 24, line 12, explicitly states that a streptavidin-coated plate purchased from Boehringer-Mannheim was used.”

appellant's specification at page 24, line 12; necessarily or inherently result in a bound monolayer of single DNA stands.⁴

According to appellant (Brief, page 9), "product literature for six (6) different commercially available streptavidin-coated surfaces," demonstrates that a monolayer is formed according to the requirements of appellant's claimed invention. In this regard, appellant directs attention to (Exhibit 1), which according to appellant (Brief, page 10), describes a streptavidin-coated product produced by Dynal Biotech. Appellant asserts (id.), "[t]he excerpt explicitly states '[a]nalysis and close calculations show that the bead-coating consists of a mon[o]layer of covalently coupled streptavidin.'" From this appellant asserts (id., emphasis removed), "the Dynal product is unquestionably a surface modified to contain a monolayer of streptavidin."

While we acknowledge appellant's assertions, as we understand it, Exhibit 1 is directed to beads coated with "a monolayer of covalently coupled streptavidin. . . ." The issue before us is not whether streptavidin is a monolayer on streptavidin coated beads, but whether the disclosure in appellant's specification of microtiter plates in appellant's specification provides support for the term "monolayer" as it is used in the claimed invention. Exhibit 1 does not address this issue, accordingly, we do not find Exhibit 1 persuasive.

⁴ Kennecott Corp. v. Kyocera Int'l, Inc., 835 F.2d 1419, 1422, 5 USPQ2d 1194, 1197 (Fed. Cir. 1987) ("By disclosing in a patent application a device that inherently performs a function, operates according to a theory, or has an advantage, a patent applicant necessarily discloses that function, theory, or advantage even though he says nothing concerning it.")

Appellant then directs attention (id.), to Exhibit 2, asserting that Promega Corporation “markets a 96-well microtitre plate of the type referenced at page 11 of the present specification. In this regard, appellants asserts (id.), “Exhibit 2 is the product insert literature for Promega’s SAM²-brand biotin capture membrane. Of particular note is that the very name of the product, SAM, is a well-known acronym for ‘self-assembled monolayer.’” Appellant refers to Exhibit 3⁵ to support the assertion that “SAM” is an art recognized acronym for “self-assembled monolayer.”

Exhibit 2 also does not relate to microtiter plates, but instead refers to a SAM²® Biotin Capture Membrane. There is no evidence on this record that this membrane is the same as a microtiter plate. Therefore, Exhibit 2 does not address the issue before us. Accordingly, we do not find Exhibit 2 persuasive.

According to appellant (id.), “[a] slew of other companies make equivalent streptavidin-coated surfaces wherein the streptavidin is in the form of a monolayer on the surface. Examples include Perkin Elmer (see Exhibit 4), Nunc (Exhibit 5), Upstate (Exhibit 6), and Roche Applied Science (Exhibit 7). . . . They are all surfaces modified to contain an immobilized streptavidin monolayer.”

While Exhibits 4-6 are directed to microtiter plates, upon review of these Exhibits we find no disclosure of whether the plates contain a streptavidin monolayer. Accordingly, we do not find Exhibits 4-6 persuasive with regard to the issue before us. See also Answer, page 16, where the examiner finds that these Exhibits “do not directly inform this analysis.”

⁵ According to appellant (Brief, page 11), “Exhibit 3 is an excerpt from the www.acronymfinder.com website,” which defines the acronym “SAM” as, inter alia, “Self-

This leaves Exhibits 7 and 8. As appellant explains (Brief, bridging paragraph, pages 9-10 and 11), as a result of from “a corporate merger/restructuring, Boehringer-Mannheim was renamed Roche Molecular Biochemicals on March 5, 1998 (see Exhibit 8 . . .), which company was then subsequently re-named Roche Applied Science. The product formerly marketed under the Boehringer-Mannheim name is now sold by Roche Applied Science under the trademark StreptaWell (see Exhibit 7).”

Upon review of Exhibits 7 and 8, we find that like Exhibits 4-6, Exhibits 7 and 8 do not disclose whether the plates contain a streptavidin monolayer. Accordingly, we do not find Exhibits 7 and 8 persuasive with regard to the issue before us. See also Answer, page 16, where the examiner finds that these Exhibits “do not directly inform this analysis.”

Having found that Exhibits 1-8 do not resolve the issue before us, we move to the remaining two pieces of evidence that appellant relies upon to support his position - the Strohner Declaration, and the Jordan reference. According to Strohner (Strohner Declaration, paragraph 2), “[r]egardless of coating procedure details, immobilization of streptavidin onto solid-surfaces (such as plastic microtiter plates and membranes) will result in a reactive streptavidin monolayer. DNA molecules which are bound to this reactive streptavidin monolayer will inevitably form a superimposed DNA monolayer.” While the examiner asserts (Answer, page 17), that weight was given to the Strohner Declaration, the opinion expressed therein is rebutted by the Jordan reference.

According to appellant (Brief, page 13, emphasis removed), “the probe DNA is explicitly stated in Jordan et al. as forming a “probe DNA monolayer.” (See Jordan et al., page 4940, right-hand column, middle of first full paragraph.)” In response, the examiner finds (Answer, page 17), “[a]ppellant ignores the plain statement of Jordan that “[t]he SPR signal resulted from hybridization onto immobilized probes is further amplified by the formation of streptavidin/DNA multilayers which grow by a combination of DNA hybridization and biotin-streptavidin binding (see abstract of Jordan).” Upon review of Jordan, we find that these statements by the examiner and appellant are both correct and are not in conflict. Further, while Jordan refers to immobilization on a gold surface and not a microtiter plate, we believe that some explanation is necessary to dispel the conflict created on this record. With reference to figure 1 of Jordan, we note that a “probe monolayer” is formed by adsorbing probe DNA onto the gold surface. Notwithstanding any other step, this first step of adsorbing probe DNA onto the gold surface results in the formation of a “probe monolayer.” Accordingly, appellant is correct. Now, in a subsequent step, biotinylated complements (e.g. biotinylated DNA) is hybridized to the probe DNA monolayer. Jordan, page 1440, second column, first full paragraph. The result is a probe DNA – biotinylated complements multilayer. Accordingly, the examiner is correct.

For illustrative purposes, let’s consider this analysis in the context of a streptavidin coated microtiter plate. Assume that a monolayer of streptavidin is coated onto a microtiter plate. Then single DNA strands are attached to the microtiter plate using streptavidin as a linker. For clarity, this means that each

single DNA strand will be attached to a single streptavidin molecule that is attached to the microtiter plate. Looking only at the DNA layer, one will see a monolayer of single DNA strands. However, looking at a cross-section of the wells of the microtiter plate, one will see a multi-layer, wherein the well forms the base, streptavidin molecule is attached to the well, and single DNA strands are attached to the streptavidin.

Now, considering page 24, lines 10-13 of appellant's specification, "PCR reaction products were mixed with an equal volume of Buffer . . . and transferred to individual wells of a streptavidin coated thin wall microtiter plate. . . ." As we understand it, the streptavidin is acting as a linker – linking the PCR reaction products to the plate. So from the examiner's point of view a multi-layer will result, if one looks at a cross-section of the microtiter plate. However, looking at each layer, Strohner (Strohner Declaration, paragraph 2), informs us that regardless of how the streptavidin plate was coated, the result will be a monolayer of streptavidin on the plate. Therefore, the "linkers" are in the form of a monolayer. When the PCR products are added to this monolayer, the result will be a monolayer of PCR products attached to the microtiter plate through a monolayer of streptavidin linkers. See Strohner Declaration, paragraph 2, "DNA molecules which are bound to this reactive streptavidin monolayer will inevitably form a superimposed DNA monolayer." Therefore, we see no conflict between the Strohner Declaration and the teachings of Jordon. The interpretations of the examiner and appellant differ only with regard to the manner in which you look at the resulting plate.

In the context of appellant's claimed invention, we find that part (a) of claim 1 to read "a complex consisting of a single DNA strand of a double stranded DNA of at least 40 base pairs containing the locus of a variation, wherein said single DNA strand is within a monolayer of single DNA strands which are bound to a solid surface. . . ." There is no requirement that the single DNA strand be attached directly to the solid surface. Part (a) of claim 1 simply requires that the single DNA strand be "bound" to a solid surface. With the benefit of the Strohner Declaration we find that single DNA strands of a double stranded DNA bound to a streptavidin coated microtiter plate, such as the one described at page 24, lines 10-13, will inherently result in a monolayer of single DNA strands as set forth in appellant's first claim. As set forth in Kennecott Corp., 835 F.2d at 1422, 5 USPQ2d at 1197, "[b]y disclosing in a patent application a device that inherently performs a function, operates according to a theory, or has an advantage, a patent applicant necessarily discloses that function, theory, or advantage even though he says nothing concerning it."

Accordingly, it is our opinion that by disclosing that PCR products can be attached to streptavidin coated microtiter plates appellant has provided sufficient descriptive support to include the term "monolayer" as done so in the claims before us on appeal. Therefore, we reverse the rejection of claims 1-5, 7-18, 20-31, 33-44, 46-52, and 67-76 stand rejected under 35 U.S.C. § 112, first paragraph.

Obviousness:

The combination of Stimpson and Wittwer:

Claims 1-5, 8, 10-18, 21, 23-31, 34, 36-44, 47, 49-52, 67-71, 73, 74, and 76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson and Wittwer.

The examiner finds (Answer, page 5), “Stimpson teaches a method of detecting DNA variation by monitoring the formation or dissociation of a complex. . . .” In this regard, the examiner finds (id.), the complex taught by Stimpson consists of:

- (a) a single strand of a DNA sequence . . . oligonucleotide are attached to a glass solid support which is a monolayer of the nucleic acids . . . ,
- (b) an oligonucleotide specific for the single stranded DNA sequence specific for one allele of the variation and capable of hybridizing to the single strand (a) to form a duplex . . .
- (c) a marker detection of the duplex structure of (a) plus (b) which forms a complex with the said duplex (here the selenium label . . .).

According to the examiner (Answer, page 6), Stimpson’s method comprises

- (1) steadily and progressively adjusting the temperature by 1°C increments . . .
- (2) continually measuring an output signal indicative of the duplex formed from the strand (a) and probe (b). . . and
- (3) recording the conditions at which a change in reaction output signal occurs which is attributable to formation or dissociation of the complex and is thereby correlated with the strength with which the probe (b) has hybridized to the single strand (a). . . .

The examiner recognizes (id.), however, that “Stimpson does not teach the use of a marker which is duplex specific in the analysis.” To make up for this deficiency, the examiner relies on Wittwer, which according to the examiner (Answer, page 6), “teaches a method of detecting DNA variation by monitoring

the formation or dissociation of a complex (abstract). . . .” In this regard, the examiner finds (Answer, pages 6-7), the complex taught by Wittwer consists of:

- (a) a single strand of a DNA sequence . . . ,
- (b) an oligonucleotide specific for the single stranded DNA sequence. . . ,
- (c) a marker specific for the duplex structure of (a) plus (b) which forms a complex with the said duplex and reacts uniquely when interacting within the duplex.

In this regard, the examiner focuses attention on the fluorescent dye SYBR green. Id.

According to the examiner (Answer, page 7), Wittwer’s method comprises:

- (1) “monitoring fluorescence while changing temperature at a rate of 0.1 degree C/second.” . . .
- (2) continually measuring an output signal indicative of interaction of the marker with duplex formed from the strand (a) and probe (b) . . . and
- (3) recording the conditions at which a change in reaction output signal occurs which is attributable to formation or dissociation of the complex and is thereby correlated with the strength with which the probe (b) has hybridized to the single strand (a)

Based on this evidence the examiner finds (Answer, bridging paragraph, pages 8-9),

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the markers of Wittwer in the mutation detection method of Stimpson since Wither states “SYBRTM Green I is a preferred double strand specific dye for fluorescence monitoring of PCR, primarily because of superior sensitivity, arising from greater discrimination between double stranded and single stranded nucleic acid. SYBRTM Green I can be used in any amplification and is inexpensive. In addition, product specificity can be obtained by analysis of melting curves” Thus, an ordinary practitioner would have been motivated to use SYBRTM Green I in the melting curve analytical method of Stimpson since Wittwer teaches that this intercalator is superior in sensitivity, is useful in the particular assay employed by Stimpson since the waveguides would detect the fluorescent label and is inexpensive.

In response appellant asserts (Brief, page 16), Stimpson “emphasize that fluorescent-based systems are insensitive and therefore provides an alternative optical wave guide system which improves sensitivity.” According to appellant (17), the optical wave guide system taught by Stimpson is completely different than using a fluorescent-based system and therefore a person of ordinary skill in the art would not have been motivated to modify Stimpson for use with a fluorescent dye like that taught by Wittwer. In addition, appellant asserts (id.), Wittwer does not suggest or employ the SYBR Green dye in a “solid-phase hybridization, which is the subject of the present claims.” In support of this assertion appellant relies on the Baldeschwieler Declaration and the Kwok Declaration.

Initially, we note that Baldeschwieler declares that he was the senior investigator and coauthor of Stimpson. Baldeschwieler Declaration, paragraph 1. In this regard, Baldeschwieler declares (Baldeschwieler Declaration, paragraph 2),

Both before and after the publication of Stimpson . . . , one skilled in the art would not expect the DNA binding capacity of any of the stable and common 2-D surfaces and chemistries to yield sufficiently strong fluorescent signals sufficiently ‘instantly’ (sub0second0 in f fluorescence based assay method to allow for dynamic tracking of signal changes in real-time, when applying practically useful rates of heating. One skilled in the art would, therefore, most rationally turn to 3-D (gel-type) arrays to solve this widely recognized problem, since the considerable 3rd dimension provides far greater capacity and scope for DNA binding and manipulation.

According to Baldeschwieler (Baldeschwieler Declaration, paragraph 3), these “known limitations of solid surface fluorescence assays . . . are repeated[ly] emphasized in the Introduction, Results, and Discussion sections of Stimpson. . . .” Similarly, Kwok explains that “[t]he methods [of Wittwer] involve the liquid phase hybridization of amplified DNA strands either with each other or with oligonucleotide probes. None of these methods would lead a worker in the field to the expectation that allelic discrimination could be achieved . . . on a solid surface”

Upon consideration of record, we find Stimpson teaches (page 6379, column 2), “[b]ecause the amount of fluorescent label on the surface of a chip is quite low, the time required to scan the array is on the order of 1 min.” As we understand this statement, if a fluorescent dye is used (as is required by appellant’s claimed invention) for every incremental increase in temperature 1 min. would be required to scan the array for fluorescence. In our opinion this is contrary to the requirement in appellant’s claim that the method comprises a steady and progress adjustment of temperature at a rate of between 0.01 to 1°C per second; and continually measuring an output signal indicative of interaction of the dye with duplex formed” To the contrary, as we understand Stimpson, the temperature would be adjusted and then it would take 1 min. for the chip to be scanned. In our opinion, this is contrary to the requirements of appellant’s claimed invention. See e.g., Stimpson (*id.*), “[m]elting curves could provide an additional dimension to the system and allow differentiation of closely related sequences. . . . However, if 1 min is required to read/wash a DNA chip,

then a high resolution melting curve from 30 to 70°C would require 40 min; i.e., measurement is rate limiting.”

In addition, Stimpson teach (id.), “[r]emoval of background signal would require some sort of washing system to eliminate the label as it dissociates from the capture site.” The examiner has does not appear to have appreciated this teaching in Stimpson which further leads away from appellant’s requirement for a steady and progressive adjustment of temperature while continually measuring output signal. As we understand it, it would be hard to meet the requirements of appellant’s claimed invention if the one has to stop and wash the array after each incremental increase in temperature.

Therefore, despite the accolades that the examiner gives to the SYBR dye taught by Wittwer, it is a fluorescent dye. As such it would appear to suffer from the same problems that Stimpson teaches as applying to fluorescent dyes. There is no evidence on this record that the use of fluorescent dyes including SYBR would not suffer the same problems that Stimpson teach as applying to fluorescent dyes in a solid state environment. Accordingly, it is our opinion that the examiner has not provided the evidence necessary to establish a prima facie case of obviousness.

As set forth in In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000):

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . Close adherence to this methodology is especially important in cases where the very ease with which the invention

can be understood may prompt one “to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.”

Most if not all inventions arise from a combination of old elements. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. [Citations omitted].

In other words, “there still must be evidence that ‘a skilled artisan, . . . with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.’” Ecolochem Inc. v. Southern California Edison, 227 F.3d 1361, 1375, 56 USPQ2d 1065, 1075-76 (Fed. Cir. 2000). At best, the statement of the rejection establishes that individual parts of the claimed invention were known in the prior art. The examiner, however, has not established that a person of ordinary skill in the art would recognize a fluorescent dye could be used in the method taught by Stimpson, while steadily and progressively adjusting the temperature at a rate of between -.1 to 1 C per second and continually measuring an output signal indicative of interaction of the dye with duplex formed. . . .” as is required by appellant’s claimed invention.

On reflection, we find that the examiner has not met his burden of establishing a prima facie case of obviousness. Accordingly, we reverse the rejection of claims 1-5, 8, 10-18, 21, 23-31, 34, 36-44, 47, 49-52, 67-71, 73, 74,

and 76 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson and Wittwer.

The combination of Stimpson, Wittwer and Heller:

Claims 1-5, 7, 8, 10-18, 20, 21, 23-31, 33, 34, 36-44, 46, 47, 49-52, and 67-76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer and Heller.

The examiner relies on the combination of Stimpson and Wittwer as set forth above. According to the examiner (Answer, page 9), the combination of Stimpson and Wittwer “do not teach immobilization of the oligonucleotide using biotin-streptavidin.” To make up for this deficiency the examiner relies on Heller. According to the examiner (id.), “Heller teaches immobilization of oligonucleotides to arrays using biotin-streptavidin for nucleic acid detection assays.” Heller, however, does not make up for the deficiencies in the combination of Stimpson in view of Wittwer.

Accordingly, we reverse the rejection of claims 1-5, 7, 8, 10-18, 20, 21, 23-31, 33, 34, 36-44, 46, 47, 49-52, and 67-76 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer and Heller.

The combination of Stimpson, Wittwer and Konrad:

Claims 1-6, 8-19, 21-32, 34-45, 47-52, 67-71, 73, 74, and 76 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer and Konrad.

The examiner relies on the combination of Stimpson and Wittwer as set forth above. According to the examiner (Answer, page 10), the combination of Stimpson and Wittwer “do not teach the use of Hepes buffer in hybridization.” To make up for this deficiency the examiner relies on Konrad. According to the examiner (id.), Konrad teaches that the “conditions for hybridization of oligonucleotide sequences are well known”, and may include a hepes buffering system. Konrad, however, fails to make up for the deficiencies in the combination of Stimpson in view of Wittwer.

Accordingly, we reverse the rejection of claims 1-6, 8-19, 21-32, 34-45, 47-52, 67-71, 73, 74, and 76 under 35 U.S.C. § 103(a) as being unpatentable over the combination of Stimpson, Wittwer, and Konrad.

REVERSED

Donald E. Adams)	
Administrative Patent Judge)	
)	
)	BOARD OF PATENT
)	
Demetra J. Mills)	APPEALS AND
Administrative Patent Judge)	
)	INTERFERENCES
)	
)	
Lora M. Green)	
Administrative Patent Judge)	

DA/dym

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