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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DAVID ZAHNISER,
MICHAEL ZAHNISER, and ADAM YIE

Appeal 2019-003127
Application 13/526,223
Technology Center 2400

Before RICHARD M. LEBOVITZ, JASON V. MORGAN, and JOHN A. EVANS, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

The Examiner rejected the claims under 35 U.S.C. § 103 as obvious. Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals from the Examiner's decision to reject the claims. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM-IN-PART.

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as Roche Diagnostics Hematology, Inc. Appeal Br. 1.

STATEMENT OF THE CASE

The Examiner rejected the claims as follows:

1. Claims 1–8, 15–18, 21–27, 29, 30, 33, 35, 36, 39–43, 48–51, and 53–61 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Yamada (US 2010/0169811 A1, published July 1, 2010) ("Yamada"), Ortyn et. al. (US 2010/0232675 A1, published Sept. 16, 2010) ("Ortyn"), and Winkelman et. al. (US 2011/0070606 A1, published Mar. 24, 2011) ("Winkelman"). Ans. 4; Office Act.[2] 5.

2. Claims 19 and 31 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Yamada, Ortyn, Winkelman, and Bacus (EP 0 549 905 A1, published July 7, 1993) ("Bacus"). Ans. 17; Office Act. 22.

3. Claims 34, 45, and 63–66 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Yamada and Ortyn. Ans. 18; Office Act. 23.

4. Claim 62 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Yamada, Ortyn, Winkelman, and Herbert (US 2003/0161003 A1, published Aug. 28, 2003) ("Herbert"). Ans. 21; Office Act. 26.

Independent claim 1 is representative and reproduced below (annotated with bracketed numbers for reference to the specific limitations in the claim):

> 1. A method of displaying images of cells in a sample, the method comprising:
>
> [1] obtaining a first set of images of a plurality of cells in the sample;
>
> [2] determining values of a property for each one of the cells based on the first set of images; and
>
> [3] displaying a second set of cell images in an ordered array on a display device,

[2] Office Action, mailed May 23, 2017.

> [4] wherein each member of the second set of cell images corresponds to and shows only one of the plurality of cells;
>
> [5] wherein each member of the second set of cell images corresponds to a different one of the plurality of cells;
>
> [6] wherein each member of the second set of cell images is ordered in the array based on the value of the property determined for the cell that corresponds to the member; and
>
> [7] wherein each one of the plurality of cells is a red blood cell or a platelet.

REJECTION BASED ON YAMADA, ORTYN

The Examiner found that Yamada describes a system for visually inspecting blood cells comprising obtaining images of cells as in the first step [1] of claim 1. Office Act. 5. The Examiner also found that Yamada determines ordering images of cells "based on the value of the property determined for the cell" as recited in limitation [6] claim. *Id.* The Examiner determined, however, that Yamada does not describe displaying a second set of images which show only one of the plurality of cells, where each image corresponds to a different cell as required by limitations [4] and [5] of the claim. *Id.* However, the Examiner found that Ortyn makes up for this deficiency and describes displaying images of a second set of single blood cells and selecting the images for the different properties they exhibit. *Id.* at 6. The Examiner determined it would have been obvious to one of ordinary skill in the art to combine Yamada and Ortyn to acquire multispectral images of single cells from a population of cells as described in Ortyn (citing paragraph 13). *Id.*

The Examiner further cited Winkelman as providing a reason to analyze red blood cells in the blood cell samples of Yamada and Ortyn, meeting limitation [7] of the claim. Office Act. 6–7.

Appellant argued 20 groups of claims separately. The arguments do not identify the specific rejection associated with the claims. We address the claims in accordance with the specific groups argued by Appellant.

To the extent that any claim is not specifically addressed, the claim stands or falls in the group in which it was argued, or with the independent claim from which it depends. 37 C.F.R. § 41.37(c)(1)(iv).

DISCUSSION

Group 1: 1–3, 6, 8, 18, 19, 21–24, 27, 29, 31, and 33

Appellant states that Yamada's disclosure describes a doctor or technician reclassifying white bloods among various white blood cell types. Appeal Br. 14. Appellant contends that the technician or doctor must take into account the nature of the cell and its "local environment," particularly if the cell metrics were obtained from overlapping cells or cells in contact with one another. *Id.* Appellant states that Yamada's images allow such an assessment, "as they show each classified white blood cell in its local environment within the sample, surrounded by additional cells." *Id.* (citing Fig. 13 of Yamada). For this reason, Appellant argues that applying Ortyn's single cell display to Yamada would "impair" Yamada's method. *Id.* at 15.

Appellant's argument does not persuade us that the Examiner erred. Appellant has not pointed to persuasive disclosure in Yamada which supports the contention that the local environment of neighboring cells is used to reclassify the cells. An argument made by counsel in a brief does not substitute for evidence lacking in the record. *Estee Lauder, Inc. v. L'Oréal, S.A.*, 129 F.3d 588, 595 (Fed. Cir. 1997). Appellant identified paragraph 137 of Yamada as support for its contention. Reply Br. 3. However, Appellant

did not point to the specific disclosure in this paragraph where the "local environment" of cells was used to reclassify the white blood cells as asserted by Appellant. As explained below, Yamada does not teach in paragraph 137 that the local environment of neighboring cells is used to reclassify the cells.

Yamada teaches that reclassification of the cells is facilitated by ordering the images by the properties used to classify the cell. Yamada ¶¶ 134–37. Yamada explains that the blood cell images in the array of images are arranged in "imaging sequence" in Fig. 19 and "in the sequence in accordance with the characteristic parameter values" in Fig. 13. Yamada ¶ 137. The "imaging sequence" is the order in which the images were obtained during the scanning of the slide. Yamada explains that by ordering cells in the array by the parameter used to classify them, such as the nucleus to cytoplasm ratio ("NC"), it is easier to find the erroneously classified cells because cells having similar nuclear shapes are in the same "vicinity" than when they are in imaging sequence,[3] allowing the user to more easily identify and compare the misclassified cells.[4]

[3] "In the screen in which the blood cell images are aligned in imaging sequence as shown in FIG. 19, the adjacent blood cell images may not have a similar shape. For this reason, the surveyor such as a laboratory technician or a doctor must carefully confirm all the blood cell images and it is impossible to easily find erroneous classifications." Yamada ¶ 137

[4] "On the other hand, in the screen in which the blood cell images are aligned in descending sequence with respect to the 'NC ratio' of the characteristic parameter as shown in FIG. 13, the blood cell images with a small NC ratio among the lymphocytes with a large NC ratio are generally arranged in the latter part. In addition, as described above, since the monocyte has a NC ratio smaller than that of the lymphocyte, the blood cell images of the lymphocyte with a small NC ratio which are arranged close to the monocyte group are approximate to the shape of the monocyte, so that

The discussion of cells being in the "vicinity" of each other (¶ 137) is reference to the array of the plurality of images, not to the individual cells in the image. This is explained in more detail below with reference to Fig. 13 of Yamada, which is copied below:

FIG.13

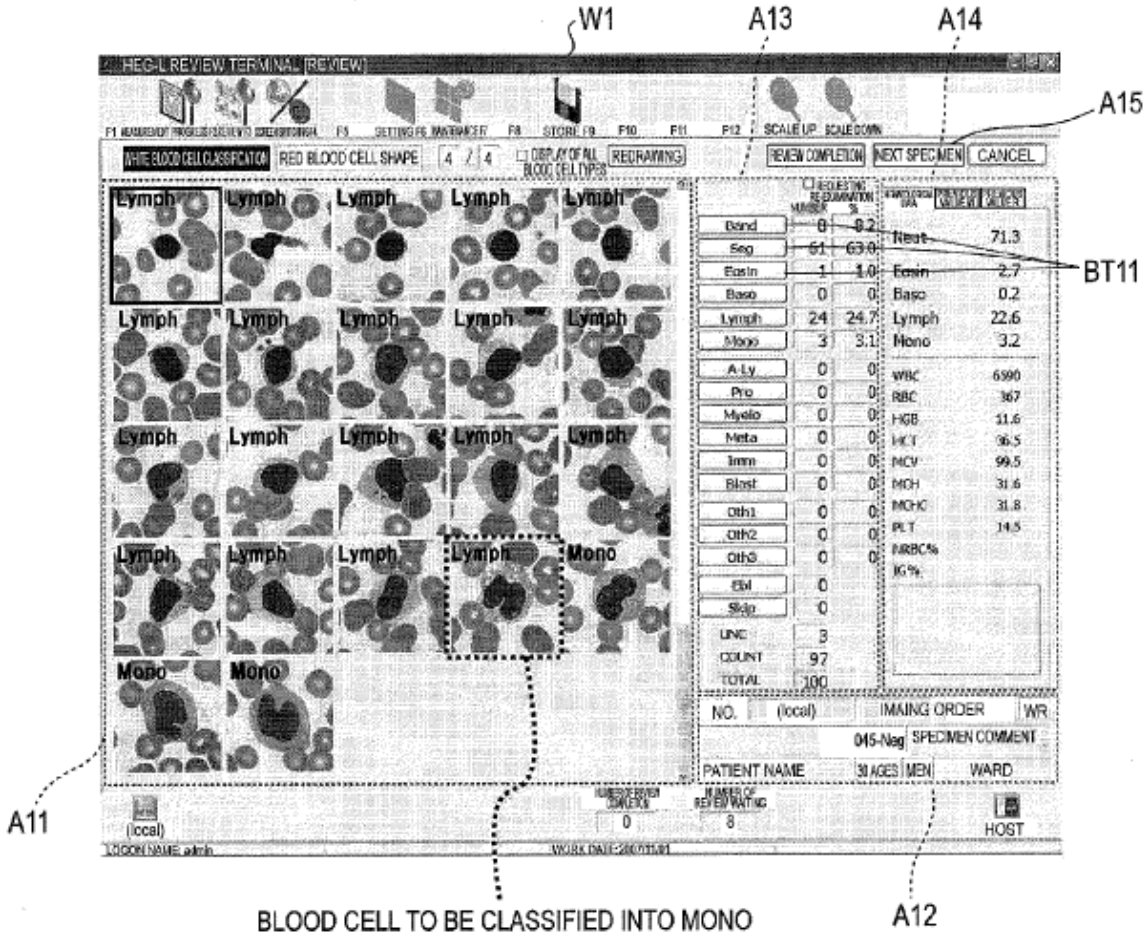

Fig. 13, reproduced above, shows an array of a plurality of images, where each image is represented by a square and shows a darkly stain cell nucleus aligned in the middle of each image. Yamada teaches that a computer obtains the images of the cells, classifies the cells, and arranges

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the blood cell images of the monocyte have a high possibility of being erroneously classified as lymphocytes." Yamada ¶ 137.

the images in sequence based on a characteristic of the cell.[5] The images are displayed in each square of Fig. 13, and the "vicinity" is the neighboring image squares. While it is true that each individual image contains a number of different cells, only one nucleus is stained and analyzed in each image. Appellant did not direct us to disclosure in Yamada, or any other fact-based evidence, where the additional cells displayed in single square image were used by Yamada to classify the cells. Thus, applying Ortyn's teaching about displaying single cells would not impair Yamada.

We further note that the Examiner relied on Yamada for a display device as illustrated in Fig. 13 reproduced above, and Ortyn for disclosing additional ways to display and sort cells. Office Act. 5–6; Ans. 22. Thus, Yamada's teaching about the advantage of sorting cells by their properties to facilitate accurate classification would be *applicable* to Ortyn's system of displaying single cells when flow cytometry is utilized to classify cells. Ortyn does not have neighboring cells because it separates single cells by flow cytometry and therefore is not impaired by Yamada's teaching of arranging cells by a property of interest.

[5] "A fourth aspect of the present invention is a computer program product comprising: a computer readable medium, and instructions, on the computer readable medium, adapted to enable a general purpose computer to perform operations comprising: (a) obtaining characteristic parameter values based on a plurality of cell images obtained by imaging a sample including the plurality of cells, wherein each of the characteristic parameter values respectively indicates characteristic of each of the cells; (b) determining types of the cells based on the characteristic parameter value obtained in the step (a); and (c) controlling the display so as to display the cell images in a sequence based on the types of the cells obtained in the step (b) and the characteristic parameter values obtained in the step (a)." Yamada ¶ 11.

Appellant also argues that the Examiner did not provide an adequate reason to combine Yamada and Ortyn. We do not agree.

The Examiner states that it would have been obvious to combine the teaching in the two publications because "having encoded thereon computer readable instructions for visual inspection of cells by fluorescence channels as taught by Ortyn to acquire dark/light field and fluorescence images . . . would allow acquire multispectral images from a population of cells" as described in Ortyn. Office Act. 6. Appellant argues that this rationale is not relevant because Yamada does not used spectral images for classification purposes, while Ortyn does. Appeal Br. 15. Appellant further states that it "would been appreciated by a person of ordinary skill in the art, Yamada's classification methods apparently perform satisfactorily without such [spectral] images." *Id.* at 15–16.

This argument does not persuade us that the Examiner erred. As we understand the Examiner's rationale, when spectral images of cells are obtained as described by Ortyn, it would have been obvious to one of ordinary skill in the art to apply Yamada's teaching about ordering cells based on the properties observed in Ortyn's spectral images. Applying Yamada to Ortyn in this way would preserve Ortyn's teaching about displaying spectral images of "only one of the plurality of cells" as recited in limitation [4] of claim 1.

Appellant also states that it "does not agree with the Office's apparent contention that in Ortyn, 'each member of the second set of cell images corresponds to a different one of the plurality of cells'" as in limitation [5] of claim 1. Appeal Br. 16. Appellant argues that there are multiple images

displayed in Ortyn of the same white blood cell, pointing to Fig. 5 of Ortyn which shows four images of each cell. Appeal Br. 16–17.

This argument is not persuasive. As discussed by the Examiner, each horizontal row in Fig. 5 of Ortyn is of a different cell. Ans. 23; Office Act. 6. In view of Yamada's teaching of ordering cells based on only a single characteristic, such as the NC ratio, it would have been obvious to one of ordinary skill in the art to arrange the single cells based only one spectral property – not all four as shown in Fig. 5. Appellant is disparaging the rejection by focusing on the disclosure in Ortyn individually, but the rejection was based on the obviousness of modifying Ortyn's teaching based on Yamada. "Non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). Thus, while Ortyn teaches in one embodiment displaying different spectral images of the same cell, Appellant has not identified any reason why it would be necessary to use each of the different spectral images, when it is desired to look at only one characteristic as taught by Yamada. Consistently, Ortyn specifically teaches analyzing only one characteristic of the population.[6] Thus, while Appellant argues it is "fundamental" to Ortyn's method to use all four images, Appellant's main support for this statement is that one of Ortyn's embodiments shows all four

[6] "The photometric and/or morphometric image features calculated from the collected images are analyzed to enable at least one characteristic of a cell or population of cells to be measured." Ortyn ¶ 14. "As noted above, in addition to collecting image data from a population of biological cells, an aspect of the concepts disclosed herein involves processing the image data collected to measure at least one characteristic associated with a disease condition in the imaged population." *Id.* at ¶ 64.

images. Appeal Br. 18. But Appellantfails to take into account the teaching that *only one characteristic* of a cell may be relevant to a determination of the cell type or condition (*see* fn. 6), and that Yamada uses only one characteristic in its analysis.

Appellant also contends that it would not have been obvious to have applied the teachings of Yamada and Ortyn to red bloods or platelets as required by claim 1 because their teachings are designed to be used for white blood cells. Appeal Br. 19.

This argument is also not persuasive. The Examiner does not suggest applying the same teachings in Yamada and Ortyn relating to white blood cell characteristics to red blood cells. For example, the Examiner specifically pointed to Winkelman's teaching about measuring hemoglobin content of the red blood cells (Office Act. 8), a property that would not be measurable in a white blood cell. Winkelman also teaches measuring red blood cell morphology.[7] We further note also Fig. 13 of Yamada reproduced above contains the heading "red blood cell shape," reasonably suggesting, along with Winkelman, that one of ordinary skill in the art had reason to apply the teachings about the characterizing the cytology of white blood cells as described in Yamada and Ortyn to red blood cells.

[7] "In an embodiment of the invention capable of preparing and analyzing cells from blood samples, the computer 300 may be able to calculate the number of a specific type of cell in a particular volume of blood, for example for blood, red cell, white cell, and platelet counts and other measured and derived components of the CBC such as: *hemoglobin content, red blood cell morphology*." Winkelman ¶ 36 (emphasis added). *See also* Winkelman ¶ 50.

Group 2: claims 4 and 25

Claim 4 and 25 are dependent claims that recite where the measured property "comprises a cell hemoglobin content." Appellant contends that Winkelman does not teach how to make the calculation regarding hemoglobin content. Appeal Br. 20. This argument is not persuasive.

An examiner is entitled to presume that the prior art is enabling, shifting the burden to patent applicant to rebut the presumption. *In re Antor Media Corp*., 689 F.3d 1282, 1287–88 (Fed. Cir. 2012). When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675 (CCPA 1980); *see also* MPEP § 2121.I (9th Edition, Revision 10.2019, Last Revised June 2020).

Winkelman discloses that "wavelengths of approximately 405–430 nm are useful for imaging a hemoglobin-only image for assessing RBC morphology and hemoglobin content." Winkelman ¶ 50. Appellant did not provide evidence that Winkelman's disclosure is insufficient to enable one of ordinary skill in the art at the time of the invention to determine the hemoglobin content of the red blood cell. Appellant therefore did not meet the burden of establishing that Winkelman is not enabling.

Group 3: claims 5 and 26

Claims 5 and 26 are dependent claims that recite where the measured property "comprises a cell volume of each of the cells." Appellant makes the same argument as for Group 2 that Winkelman is not enabling for determining cell volume. Appeal Br. 21. Winkelman discloses measuring

mean corpuscular volume using cell cytometry (at ¶ 4) and Ortyn also discloses that a morphological characteristic that can be measured is cell volume (at ¶¶ 74, 80). Ortyn uses flow cell cytometry (at ¶ 53). Appellant has not met the burden of establishing the determining cell volume by flow cytometry is not enabled at the time of the invention, particularly when two publications cited in the rejection state that it can be measured. *See Sasse*, 629 F.2d 675.

Group 4: claim 7

Claim 7 is a dependent claims that recite where the measured property "comprises an optical density of each of the cells." While Appellant acknowledges that Winkelman describes measuring optical density, Appellant contends that neither Winkelman, Yamada, nor Ortyn disclose or suggest "actually ordering images based on optical density." Appeal Br. 22.

This argument is not persuasive. The Examiner relied on Yamada for teaching ordering cells based on their properties. Winkelman teaches one such property. Office Act. 9. It would have been obvious to one of ordinary skill in the art to order cells by any useful property for classification and diagnostic purposes.

Group 5: claim 15

Claim 15 depends from claim 1 and further recites "comprising detecting a disease condition in a patient based on the second set of cell images." Appellant argues that Winkelman's disclosure about determining viral and infected cells in a sample is "purely aspirational." Appeal Br. 22–23.

While we agree with Appellant that there is limited disclosure in Winkelman about detecting disease based on images of red blood cells, Winkelman discloses measuring hemoglobin content of cells (at ¶ 50) and one of ordinary skill in the art at the time of the invention, such as the doctor or technician examining the data, would know that a cell has a normal range of hemoglobin, and a content outside the normal range would be indicative of a disease. See, *e.g.*, Spec. 27–28 which indicates acceptable ranges for hemoglobin. It is commonsense that Winkelman describes measuring the hemoglobin content of red blood cells because it is indicative of the health of a red blood cell. While Winkelman does not expressly state such a reason, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton." *KSR Int'l Co. v. Teleflex Inc*., 550 U.S. 398, 421 (2007). Thus, Winkelman reasonably suggests that such measurements, when made to red blood cells, would be useful to detect a disease condition in a patient.

Group 6: Claims 16, 17, and 30

Claims 16, 7, and 30 are dependent claims that recite analyzing the images for inclusions, such as size, shape and number. The Examiner found, citing paragraphs 14 and 59, that Winkelman describes measuring inclusions in a cell. Office Act. 11.

Appellant contends that neither Winkelman, Yamada, or Ortyn disclose or suggest "actually ordering cell images in an array based on a property of inclusions, nor any specific examples of such inclusion properties such as size, shape, or number." Appeal Br. 23. This argument is not persuasive because the Examiner relied on Yamada for teaching of ordering cells by their characteristics, making it obvious to order cells by

any desired characteristic. Appellant did not identify a defect in the Examiner's reasoning.

Group 7: claims 34, 41, 43, 45, 50, 62, and 64

Independent claim 34 recites that "each member of the second set of cell images corresponds to one of the plurality of cells and is displayed as a user-selectable control on the display device" and that when "when one of the user-selectable controls is selected, the method further comprises displaying a third image on the display device." The third image is recited in the claim to be a different field of view than the second image and "showing the cell associated with the selected control and one or more neighboring cells in the sample."

The Examiner found that Ortyn's disclosure of a dot plot in Figure 5 represents neighboring cells in the sample. Office Act. 24.

Appellant contends that the Examiner's finding is erroneous. Appeal Br. 26. Appellant argues:

> [T]he collection of "dots" in in plot 59a is not a "third image" or even an "image" at all. Instead, each of the dots in plot 59a represents a point in a two dimensional feature space, where the features correspond to the x- and y-axis values. Clustering of the dots in the two dimensional feature space allows the different groups of dots to be assigned to different types of white blood cells. Thus, while each dot in plot 59a *represents* a particular white blood cell with particular values of the features on the x- and y-axes, the dots are not "images" of cells. There is no image information associated with any of the dots, nor is there a "field of view" associated with the dots. To the contrary, each dot is a zero-dimensional marker in a scatter plot (i.e., plot 59a), with no spatial extent.

Appeal Br. 26.

We agree with Appellant. As discussed by Appellant, Fig. 5 of Ortyn shows a dot plot representing clusters of cells, grouped by a property of the cell indicative of their cell type. As explained in Ortyn, "dot plot 59b (displayed at the center right of FIG. 5) substitutes a nuclear texture parameter, 'nuclear frequency' for CD45 expression on the x-axis, revealing a putative NK cell population (purple in a full color image)." Ortyn ¶ 116. There is no showing of "one or more neighboring cells in the sample" as required by the claim. The cluster do not represent neighboring cells, but rather represent properties of cells with no spatial information as to the cell's location.

The rejection of claim 34 is reversed; dependent claims 41, 43, and 64 are reversed as well. Independent claim 45 has the same limitation as claim 34 with respect to the third image and is reversed as well; dependent claim 50 is also reversed.

Appellant grouped claim 62 into Group 7. However, claim 62 depends from claim 1 and does not require a third image as in claim 34. The rejection of this claim is, therefore, affirmed because Appellant did not explain why it was separately patentable from claim 1.

Group 8: claim 35

Claim 35 depends from claim 34. The rejection of this claim is therefore reversed for the same reason as claim 34.

Group 9: claim 36

Claim 36 depends from claim 34. The rejection of this claim is therefore reversed for the same reason as claim 34.

Group 10: claims 39 and 48

Claims 39 and 48 depend from claims 34 and 45, respectively. The rejection of these claims is therefore reversed for the same reason as claims 34 and 45.

Group 11: claim 40 and 49

Claims 40 and 49 depend from claims 34 and 45, respectively. The rejection of these claims is therefore reversed for the same reason as claims 34 and 45.

Group 12: claim 42

Claim 42 depends from claim 34. The rejection of this claim is therefore reversed for the same reason as claim 34.

Group 13: claim 51

Claim 51 depends from claim 45. The rejection of this claim is therefore reversed for the same reason as claim 45.

Group 14: claims 53, 54, 58, and 59

Claim 53, depends from claim 1, and further comprises "displaying a graphical representation of a distribution of the values of the property on the display device."

The Examiner found that Ortyn discloses a histogram in Figure 8 which is a graphical representation. Office Act. 15. Appellant contends that

"while Ortyn constructs the histograms shown in Figs. 8C–8M, nothing in Ortyn suggests that such histograms are actually displayed." Appeal Br. 33.

This argument is not persuasive. Ortyn reproduces histograms in Figs. 8D–8M. Ortyn ¶ 128. The computer has a display. *Id.* at ¶ 35. Ortyn discloses that the computer "may be able to display numerical data, cell population histograms, scatterplots, and direct assessments of cellular morphology using images of blood cells displayed on the monitor." *Id.* at ¶ 36. Thus, it evident that histograms are "actually displayed" on the computer monitor of Ortyn.

The rejection of claim 53 is therefore affirmed. Appellant did not provide separate arguments for claims 54, 58, and 59. These claims fall with claim 53. 37 C.F.R. § 41.37(c)(1)(iv).

Group 15: claim 55

Claim 55 depends from claim 53 and further recites:

> wherein each image in the second set of cell images is displayed as a user-selectable control on the display device, and wherein each user-selectable control is configured so that, when selected, a marker is displayed on the graphical representation at a position corresponding to a value of the property of the cell associated with the selected control.

The Examiner found that Ortyn describes this additional limitation at paragraph 116. Office Act. 16. Appellant contends that "this portion of Ortyn merely states that when an image in Ortyn's gallery is selected, the corresponding dot in dot plot 59a is highlighted. But highlighting an existing dot in plot 59a is not the same as displaying a marker that did not already exist." Appeal Br. 34.

We are not persuaded by Appellant's argument that the Examiner erred. Appellants admits that when a cell is selected, a dot in the dot plot is highlighted.[8] The highlighting therefore serves as a marker for the position of the cell in in dot plot 59a; the highlighting of the spot is not present until the cell is selected and therefore "does "not already exist" until the selection is made. Accordingly, the rejection of the claim is affirmed.

Group 16: claim 56

Claim 56 depends from claim 53 and further recites "comprising displaying an expected distribution of the values of the property on the graphical representation of the distribution." The Examiner cited Fig. 9 of Ortyn as meeting this additional limitation. Office Act. 17.

Appellant argues that Fig. 9 shows abundance data which is actual, measured data and not an expected distribution. Appeal Br. 35.

Appellant's argument is unpersuasive because Ortyn's Figure 10B illustrates the comparison of scatter plot data, such as that illustrated in Ortyn's Figure 9, with a "CD45 bivariate plot[] for normal peripheral blood mononuclear cells." Ortyn ¶ 134. That is, Ortyn's Fig. 10B shows the distribution of "normal PBMC"—an expected distribution of normal cells—with an overlaid second distribution of mammary carcinoma cells. *Id.* ¶ 45. The image showing the expected distribution of normal cells superimposed on the distribution of carcinoma cells illustrates "how the distribution of mammary carcinoma cells is distinguishable from the distribution of the normal PBMC cells." *Id.* The claim does not require how the "expected

[8] "Cell imagery can be selected to highlight the corresponding dot in every plot in which that cell appears." Ortyn ¶ 116.

distribution" is determined. Thus, Appellant's argument that Ortyn shows "actual, measured data" does not distinguish the claim for Ortyn's disclosure. In addition, while the expected distribution is graphical, it represents values and therefore meets the limitation of "an expected distribution of the values of the property."

Nonetheless, we also consider the recited limitation of threshold values to be non-functional descriptive matter under the printed matter doctrine, which are therefore inadequate to distinguish the claimed subject matter from the prior art. *In re Ngai*, 367 F.3d 1336 (Fed. Cir. 2004); *In re Gulack*, 703 F.2d 1381, 1385 (Fed. Cir. 1983).

Group 17: claim 57

Claim 57 depends from claim 53, and further recites "comprising displaying upper and lower threshold values of the property on the graphical representation of the distribution, wherein the upper and lower threshold values define a range of values of the property that are expected for a patient."

The Examiner found that Ortyn discloses Table 1 with threshold values as recited in the claim. Office Act. 18. *See also* Office Act. 21 describing the display of expected values for claims which depend from claim 57. Appellant argues that Table 1 does not contain threshold values and they are not displayed on the graphical representation of the distribution.

We agree with Appellant that Table 1 of Ortyn, which is "an exemplary listing of exemplary photometric and morphometric definitions that can be identified for every image" (Ortyn ¶ 116), does not alone meet the claim limitation. However, the table lists "threshold" under "user-defined

masks," indicating that thresholds may be determined and used. Consistently, Ortyn specifically discloses drawing a "gate" in Fig. 8B around an area of cells, "being sufficiently large to exclude debris, and the aspect ratio being greater than −0.5, which eliminates doublets and clusters of cells." *Id.* at ¶ 126. The "gate" serves as a threshold to include cells while excluding inclusions. *See* Office Act. 21 for discussion of the gate in Figs. 8B and 9.

Values are also displayed side by side the images in Yamada (*see, e.g.,* Fig. 13 showing "Hgb," "MCV," etc.). Thus, the display of any value would have been obvious to one of ordinary skill in the art, including the gate values described in Ortyn.

Nonetheless, we also consider the recited limitation of threshold values to be non-functional descriptive matter under the printed matter doctrine, which are therefore inadequate to distinguish the claimed subject matter from the prior art. *In re Ngai*, 367 F.3d 1336 (Fed. Cir. 2004); *In re Gulack*, 703 F.2d 1381, 1385 (Fed. Cir. 1983).

Group 18: claims 60 and 61

Claim 60, which depends from claim 57, further recites "for each cell having a value of the property that falls outside the expected range of values, displaying the corresponding member of the second set of cell images in a highlighted display modality in the ordered array."

The Examiner cited Fig. 9 of Ortyn as showing a gate (the "threshold" of the claim) and for displaying cells in the array. Office Act. 21. Fig. 9 is copied below:

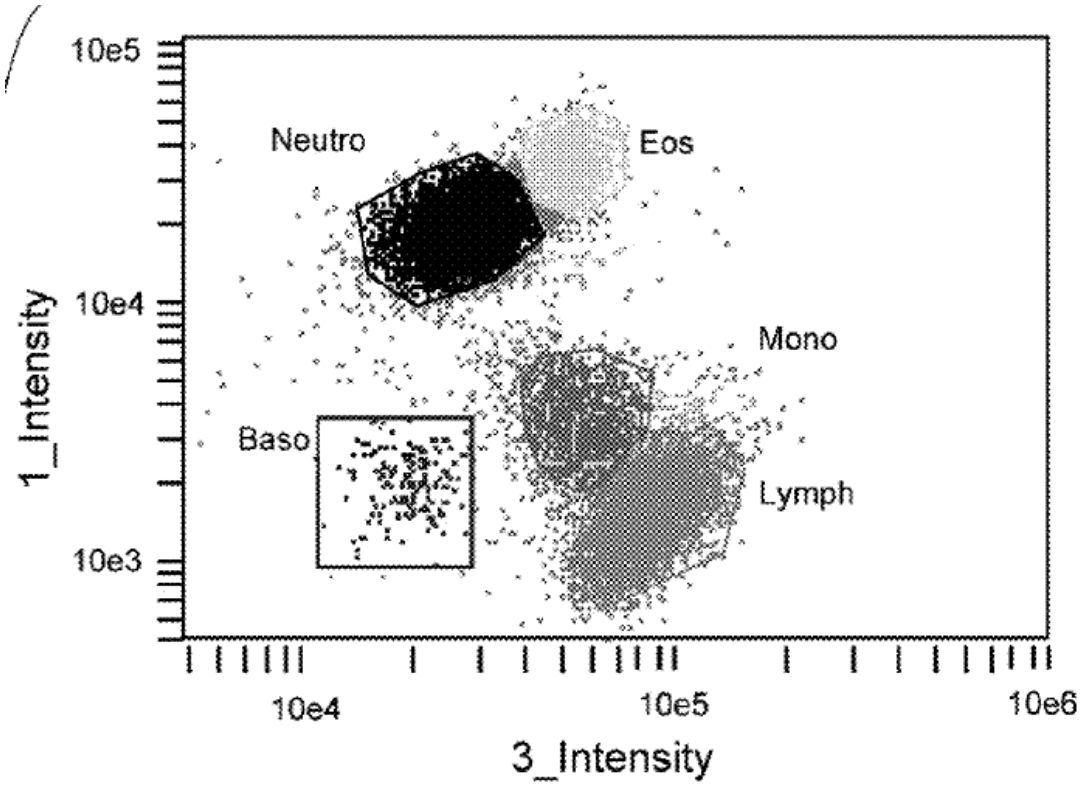

Fig. 9, reproduced above, shows CD45 marker expression on various cell types and how the relative abundance of this marker allows the cells to be separated into distinct cell type populations ("Neutro," "Eos," "Baso," etc.). A gate (the square box in the figure) is drawn around "Baso," which represents the basophils.

As explained in paragraph 126 of Ortyn (with respect to Fig. 8B which shows the same type of data), the gate separates single cells from debris, doublets, cell clusters, etc. Ortyn explains that the "veracity of the gating was tested by examining random cells both within and outside of the gate using the click-on-a-dot visualization functionality." Ortyn ¶ 126. When a dot in the dot plot is selected, an image that corresponds to the dot is displayed, allowing the user to visualize the image and verify that the dot represents a cell, debris, etc. Thus, the claim limitation reciting "for each cell having a value of the property that falls outside the expected range of

values" is met because the gate is a threshold that defines properties inside and outside of the expected range of values, i.e., single cells, debris, doublets, cell clusters. The further requirement of the claim of "displaying the corresponding member of the second set of cell images in a highlighted display modality in the ordered array" is also met because of the "click on-dot functionality."

Appellant contends that the clicking on the dots "has nothing whatever to do with particular cells having a value of a property that falls outside an expected range of values." Appeal Br. 36. However, this does not address Ortyn's explicit disclosure of a gate drawn around the population of cells which displays the expected threshold for single cells. Ortyn ¶ 126.

Appellant also raises the issue of a "third image," but the claims do not require it. Appeal Br. 37. Thus, Appellant is arguing a limitation that does not appear in the claim.

Appellant also contends the plots shown in Figs. 8B and 9 "are not the 'second set of images' either, and the borders or 'gates' that establish the population boundaries in these figures do not correspond to boundary elements that highlight *individual cells* when those cells have a value of a property that falls outside an expected range of values." Appeal Br. 37.

This argument is not persuasive. The dots in the figures were not identified by the Examiner as images; rather the Examiner specifically cited paragraph 126 of Ortyn which describes selecting a dot inside or outside the gate to display the corresponding image. Office Act. 20–21. Appellant is incorrect about what the gates show. Ortyn, as discussed above, discloses that the gates define the boundary or threshold values for single cells: dots within the gate meet the threshold and are single cells; dots outside the gate

do not meet threshold are not single cells. Ortyn ¶ 126.[9] The claim does not require that the cells outside the gate threshold are "individual cells" as asserted. Thus, cells doublets and clusters outside the gate meet the claim limitation of cells outside the threshold value.

The rejection of claim 60 is affirmed. Appellant argued claim 61 in the same grouping and it therefore falls for the same reason.

Group 19: claim 65

Claim 65 depends from claim 34. The rejection of this claim is therefore reversed for the same reason as claim 34.

Group 20: claim 66

Claim 66 depends from claim 34. The rejection of this claim is therefore reversed for the same reason as claim 34.

[9] "A gate (not separately shown) was drawn around the population containing putative single cells based on the criteria of the area being sufficiently large to exclude debris, and the aspect ratio being greater than -0.5, which eliminates doublets and clusters of cells. The veracity of the gating was tested by examining random cells both within and outside of the gate using the click-on-a-dot visualization functionality." Ortyn ¶ 126 (Discussing Fig. 8B; Fig. 9 shows the gate.)

CONCLUSION

In summary:

Claims Rejected	35 U.S.C. §	References	Affirmed	Reversed
1–8, 15–18, 21–27, 29, 30, 33, 35, 36, 39–43, 48–51, 53–61	103	Yamada, Ortyn, Winkelman	1–8, 15–18, 21–27, 29, 30, 33, 53–61	35, 36, 39–43, 48–51
19, 31	103	Yamada, Ortyn, Winkelman, Bacus	19, 31	
34, 45, 63–66	103	Yamada, Ortyn		34, 45, 63–66
62	103	Yamada, Ortyn, Winkelman, Herbert	62	
Overall Outcome			1–8, 15–19, 21–27, 29, 30, 31, 33, 53–62	34–36, 39–43, 45, 48–51, 63–66

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED-IN-PART