

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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

Appeal No. 2005-2663
Application No. 10/140,323

ON BRIEF

Before BARRY, SCHEINER, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of using gene expression data to calculate which genes regulate each other. The examiner has rejected the claims as indefinite, lacking written description, and anticipated. We have jurisdiction under 35 U.S.C. § 134. We reverse all of the rejections except the indefiniteness rejection of claim 7.

Background

The specification discloses a method for analyzing “gene perturbation data”; i.e., data resulting from “experimental manipulation of gene activity.” See pages 5-6. A gene perturbation may be a mutation or deletion that eliminates expression of a gene.

Figures 1B and 1C are, respectively, the “adjacency list” and “accessibility list” of the genetic network of Figure 1A. An adjacency list (abbreviated Adj) is a list of genes whose activities directly influence each other; “[o]ne might also call it the list of direct regulatory interactions. It completely defines the structure of the network.”

Specification, page 11. An accessibility list (abbreviated Acc) “shows all nodes (genes) that can be accessed (influenced in their activity state) from a given node by following paths of direct interactions. In the context of a genetic network, one might also call it the list of perturbation effects or the list of regulatory effects.” Id.

Figures 1B and 1C are reproduced below:

| B | | C | |
|----------|-------|----------|-----------------------------------|
| 0: | 16 | 0: | 2 16 |
| 1: | | 1: | |
| 2: | | 2: | |
| 3: | 2 5 8 | 3: | 0 2 5 8 12 14 16 |
| 4: | | 4: | |
| 5: | 12 | 5: | 0 2 12 14 16 |
| 6: | 5 12 | 6: | 0 2 5 12 14 16 |
| 7: | 2 17 | 7: | 2 8 17 |
| 8: | | 8: | |
| 9: | 10 15 | 9: | 0 1 2 5 6 10 12 14 15 16 18 20 |
| 10: | 1 20 | 10: | 0 1 2 5 6 12 14 16 18 20 |
| 11: | 20 | 11: | 0 2 5 6 12 14 16 18 20 |
| 12: | 14 | 12: | 0 2 14 16 |
| 13: | 8 17 | 13: | 8 17 |
| 14: | 0 | 14: | 0 2 16 |
| 15: | 0 | 15: | 0 2 16 |
| 16: | 2 | 16: | 2 |
| 17: | 8 | 17: | 8 |
| 18: | | 18: | |
| 19: | 8 | 19: | 8 |
| 20: | 6 18 | 20: | 0 2 5 6 12 14 16 18 |

Fig. 1

Figure 1B is a list of the genes in the network and the genes that each of them directly affects. Figure 1C is a list of the genes in the network and the genes that each of them directly or indirectly affects. Thus, for example, Figure 1A shows that gene 14

regulates gene 0, which regulates gene 16, which regulates gene 2, so the adjacency list of gene 14 is 0 and the accessibility list of gene 14 is 0 2 16. “Generating the list in Figure 1C from 1A or 1B is straightforward. The present invention addresses the more difficult problem of reconstructing all direct interactions in a network from all indirect ones, that is, to reconstruct 1A (Adj) from 1C (Acc), and to do that automatically for very large networks comprising thousands of genes.” Specification, page 11.

Discussion

1. Claim construction

Claims 1-7, 9, 16, 17, 19, and 20 are on appeal. Claims 8, 11-15, and 18 are also pending but have been withdrawn from consideration. See the Appeal Brief, page

2. Claim 1-4 are representative of the appealed claims and read as follows:

1. A method for determining all direct and indirect genetic interactions in a graph representation of a genetic network of an organism, comprising:

obtaining a first accessibility list of said graph representation of said genetic network from appropriate genetic perturbation data;

applying graph theory mathematics to the first accessibility list and its graph to determine a condensation of the graph as defined by the condensation’s accessibility list;

applying graph theory mathematics to the condensation’s accessibility list to determine an adjacency list characterizing all direct and indirect genetic interactions in said genetic network.
2. The method of claim 1, wherein said graph theory mathematics are applied using a recursive algorithm.
3. The method of claim 2, wherein said recursive algorithm determines the adjacency list of a most parsimonious graph.
4. The method of claim 2, wherein said recursive algorithm determines a list of the longest path of said graph.

Thus, claim 1 is directed to a method for determining the adjacency list of a graph representation of a genetic network by starting with an accessibility list derived from genetic perturbation data, applying graph theory mathematics to determine a condensation of the genetic network graph,² and applying graph theory mathematics to the condensation's accessibility list.

Claim 2 adds the limitation that a recursive algorithm is applied. Claim 3 adds the further limitation that the algorithm determines the adjacency list of the "most parsimonious graph," i.e., the simplest set of regulatory interactions that will fully explain the accessibility list. See the specification, page 14 and Figure 7.

Claim 4 depends from claim 2 and adds the limitation that the algorithm determines the longest path of the graph. "Paths are sequences of edges connecting adjacent nodes." Specification, page 6. Thus, the longest path in the graph would represent the longest series of regulatory interactions between genes in the network; "[a] by-product of the algorithm [that calculates the maximum path] is the adjacency list of each node." Page 41.

2. Definiteness

The examiner rejected claims 6 and 7 under 35 U.S.C. § 112, second paragraph, as being indefinite. Claim 6 depends from claim 4 and recites a series of steps in pseudocode that are implemented in the recursive algorithm. The examiner reasoned that "the last line of claim 6 recites a list of G which causes the claim to be vague and

² A "condensation" of a graph is derived by "collaps[ing] all nodes that are part of a cycle." Specification, page 13. A cycle in a genetic network is a set of genes that all influence each other (directly or indirectly). Thus, perturbing any one gene in the cycle affects all of them: "Single gene perturbations cannot resolve gene orders in a cycle." Page 12. Therefore, all the genes in a cycle must be condensed to a single

indefinite because said list of G does not list the longest path as required by the recursive algorithm of claim 4 for determining a list of the longest path.” Examiner’s Answer, pages 3-4.

The examiner’s concern seems to be that the algorithm set out in claim 6 defines a variable G to be “the genetic network graph” while the preamble of claim 1 states that the method “determin[es] . . . genetic interactions in a graph representation of a genetic network.” The examiner argues that, while “the meaning of the phrase ‘graph representation of a genetic network’ overlaps somewhat with the meaning of the phrase ‘genetic network graph’[,] . . . [they are not] identical to clearly define the metes and bounds of the claimed invention.” Examiner’s Answer, page 4.

Appellant argues that “the terms ‘graph representation of a genetic network’ and ‘genetic network graph,’ as they are used in this patent application, are synonymous. Appellant respectfully submits that persons having ordinary skill in the art would have no trouble discerning that these two terms mean the same thing.” Appeal Brief, page 8.

We will reverse this rejection. “The definiteness inquiry focuses on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the rest of the specification.” Union Pacific Resources Co. v. Chesapeake Energy Corp., 236 F.3d 684, 692, 57 USPQ2d 1293, 1297 (Fed. Cir. 2001). Claims are in compliance with 35 U.S.C. § 112, second paragraph, if “the claims, read in light of the specification, reasonably apprise those skilled in the art and are as precise as the

“strong component” before applying the algorithm that calculates the adjacency list of the network. Page 13.

subject matter permits.” Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94-95 (Fed. Cir. 1987).

Here, the phrases in question seem on their face to mean the same thing, Appellant has stated on the record that they mean the same thing, and the examiner has provided no reasoned basis on which to conclude that they mean different things. The mere fact that the dependent claim uses slightly different phrasing to refer to the same limitation does not automatically make the phrasing indefinite. The examiner has not adequately explained why those skilled in the art would be unable to determine the boundaries of claim 6 and we therefore reverse the rejection of that claim under 35 U.S.C. § 112, second paragraph.

The examiner also rejected claim 7 as indefinite. Claim 7 depends from claim 2 and adds the limitation that the condensation is determined via an algorithm that implements a series of steps that are recited in pseudocode. The examiner reasoned that “the method is directed to determining a condensation of the graph, which is directed via its dependence from claim 2 to a recursive algorithm. G^* is defined as the condensation of graph G . However, claim 7 is vague and indefinite because the algorithm of said claim via claim 2 does not result in the production of G^* .” Examiner’s Answer, page 4.

Appellant concedes that “the clarity of claim 7 can be improved by removing from the preamble mention of producing condensation of the graph.” Appeal Brief, page 9. Appellant submitted an amendment intended to accomplish this objective and overcome the rejection. See the amendment received December 23, 2004. The examiner denied entry of the amendment. See the Advisory Action mailed March 3, 2005.

Appellant does not dispute that the claim as currently written is indefinite. The amendment that was submitted to rectify the indefiniteness has not been entered. We therefore affirm the rejection of claim 7 under 35 U.S.C. § 112, second paragraph.

3. Written description

The examiner rejected claims 5 and 20 under 35 U.S.C. § 112, first paragraph, as lacking adequate descriptive support in the specification. The examiner argues that specific limitations in these claims are new matter:

8. Claim 5, last two lines, recites the new amended limitation of “and component [j] . . . by nodes j”, [which] has not been found in the instant specification. It is noted that the instant specification discloses “a data structure component [i] which is an array indexed by the nodes i of G” (page 28, [117]).

9. Claim 20, line 2, recites the limitation[s] of biotic and abiotic environmental stress, which have not been found in the instant specification.

Examiner’s Answer, pages 5-6

Regarding claim 5, Appellant argues that the holding variable j was used in original claim 7. Appeal Brief, page 10. Appellant also argues that

the letters “i” and “j” are used in the context of this patent application as holding variables for the purpose of incrementing through a recursive algorithm. These letters have no special significance other than to facilitate the repetitive action of the recursive algorithm as the value represented by the holding variable (i, j, or any other convenient symbol) increments with each repetition.

Id., pages 10-11. Regarding claim 20, Appellant argues that the specification describes exemplary types of biotic and abiotic stresses and therefore adequately describes the limitation at issue.

We will reverse this rejection. To satisfy the written description requirement, the specification need not contain the identical words used in the claims. See Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) (“[T]he disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.”). The written description requirement is satisfied in the disclosure conveys with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See id.

With respect to claim 5, the limitation that is of concern to the examiner reads as follows: “component[j] is a data structure which is an array indexed by nodes j.” The specification discloses an algorithm identical to that recited in claim 5 (see Figure 11) but does not specifically define what is represented by component[j]. As the examiner noted, however, the specification states that the algorithm “uses a data structure component[i] which is an array indexed by nodes i of G.” Page 28. Appellant argues, and the examiner does not dispute, that those skilled in the art recognize the “i” and “j” letters as mere holding variables.

In view of that understanding, those skilled in the art would understand the specification’s definition that “data structure component[i] . . . is an array indexed by nodes i of G” to be generic to any “component[]”. That is, the definition given in the specification would have been understood to apply generically to the Figure 11 algorithm: “data structure component[] . . . is an array indexed by nodes _ of G.” Since the holding variable has no special significance, we agree with Appellant that the specification adequately describes the limitation at issue in claim 5.

Regarding claim 20, the examiner argues that the specification does not describe the limitation “biotic and abiotic environmental stress”. It is true that the specification does not contain this phrase, in those words. The specification does, however, refer to “different environmental conditions” generally, as well as recite examples of both biotic and abiotic stresses.³ See pages 3-4: the claimed method can “reconstruct networks of gene interactions that change in different environmental conditions,” “identify pathways for host defense in plants,” “identify gene pathways in plants responsible for insecticidal activity,” and “identify pathways in plants that are responsible for drought tolerance and virulence.” See also page 35: the “invention will answer a multitude of questions about the genetic architecture of organisms such as . . . in different environmental conditions.”

We agree with Appellant that the examiner has not adequately explained why these specific and generic descriptions are inadequate to show possession of the method of claim 20 to a person of ordinary skill in the art. We therefore reverse the rejection for lack of adequate written description (new matter).

3. Obviousness

The examiner rejected claims 1-4, 9, 16, 17, 19, and 20 under 35 U.S.C. § 102(a) as anticipated by Küffner.⁴ The examiner’s reasoning with respect to claim 1 is as follows:

Kuffner et al. disclose a method and system, PETRI nets, for representing differential content of individual databases (KEGG and BRENDA pathway databases), comparing genomic and network information; and defining

³ A biotic stress is one that is “caused or produced by living things,” and an abiotic stress is one “not biotic”; i.e., not caused by living things. Merriam-Webster’s Collegiate Dictionary, Deluxe Edition (1998).

⁴ Küffner et al., “Pathway analysis in metabolic databases via differential metabolic display (DMD),” Bioinformatics, Vol. 16, pp. 825-836 (2000).

and analyzing paths and pathways as directed to genetic interactions data from DNA chip wherein said data is derived from disease state type of perturbation data (pages 825-826, Introduction § and Figures 2, 3, 11, and 12). The said method comprises constructing graphs from data derived from a plurality of databases wherein alias lists for the elements from said plurality of databases (page 827, column 1, line 30 to column 2, line 19). For example, SWISSPROT may be used for referencing protein coding genes (page 826, column 2, lines 13-24), as in instant claims 1 and 9.

Examiner's Answer, pages 7-8.

Appellant argues that Küffner does not anticipate because it does not disclose all the limitations of the claims, pointing specifically to the "perturbation data" and "adjacency list" limitations of the independent claims. See the Appeal Brief, pages 12-15.

The standard under § 102 is one of strict identity. "[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference." Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1576, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). If a limitation of the claimed invention is not present, either expressly or inherently, in the prior art reference, the claim is not anticipated.

In this case, the examiner's explanation of the rejection does not address many of the limitations of claim 1. The examiner has pointed to Küffner's "constructing graphs from data derived from a plurality of databases." Examiner's Answer, page 7. This might (or might not) represent a "graph representation of a genetic network" as recited in claim 1. But the examiner has not explained where Küffner discloses "obtaining a first accessibility list of [a] graph representation of a genetic network from appropriate genetic perturbation data," or "determin[ing] a condensation of the graph," or "applying

graph theory mathematics . . . to determine an adjacency list characterizing all direct and indirect genetic interactions in said genetic network.”

We have reviewed Küffner but do not find a disclosure therein of a method meeting the limitations of claim 1. As we understand Küffner, it discloses a method of analyzing data pertaining to a metabolic pathway; i.e., a series of chemical reactions catalyzed by enzymes that convert a starting material into a final product. See, e.g., Figures 11 and 12. Thus, as we understand them, the nodes in the graph shown in Küffner’s Figure 12 represent different chemical compounds and the edges represent chemical reactions (or the enzymes that catalyze them).

Küffner states that a “metabolic display (MD) (e.g. Figure 12) is a PETRI net, which exhibits in a compact (though redundant) way the space of all pathways between given source and sink in a network compatible with a set of constraints.” In other words, the PETRI net disclosed by Küffner is designed to show all the possible paths that a molecule could travel as it was converted from a starting material (source) into a final product (sink), and thereby present a more realistic view of what actually happens in biological systems than is given by the simplified metabolic pathways usually presented in textbooks (and in Küffner’s Figure 11). Therefore, the method disclosed by Küffner does not appear to be one that would act on data in the way defined by claim 1 on appeal, nor does it appear to generate “an adjacency list characterizing all direct and indirect genetic interactions in [a] genetic network.”

The examiner has not adequately explained how the cited reference discloses all the limitations of the claimed method and the limitations are not apparent to us. We therefore reverse the rejection under 35 U.S.C. § 102(a).

Summary

We reverse the rejection of claim 6 for indefiniteness, the rejections of claims 5 and 20 for lack of adequate written description, and the rejection of claims 1-4, 9, 16, 17, 19, and 20 for anticipation. However, we affirm the rejection of claim 7 for indefiniteness.

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

| | | |
|-----------------------------|---|-----------------|
| Lance Leonard Barry |) | |
| Administrative Patent Judge |) | |
| |) | |
| |) | |
| |) | BOARD OF PATENT |
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