



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
14/897,459	12/10/2015	Jiye Shi	15-1973-WO-US	5744
20306	7590	01/21/2020	EXAMINER	
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP			BORIN, MICHAEL L	
300 S. WACKER DRIVE			ART UNIT	
32ND FLOOR			PAPER NUMBER	
CHICAGO, IL 60606			1631	
			MAIL DATE	
			DELIVERY MODE	
			01/21/2020	
			PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JIYE SHI, TERENCE SEWARD BAKER,
ALASTAIR DAVID GRIFFITHS LAWSON, and
XIAOFENG LIU¹

Appeal 2019-001324
Application 14/897,459
Technology Center 1600

Before JEFFREY N. FREDMAN, JOHN G. NEW, and
JAMIE T. WISZ, *Administrative Patent Judges*.

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

¹ We use the word “Appellant” to refer to the “applicant” as defined in 37 C.F.R. § 1.142. Appellant identifies UCB Biopharma SPRL as the real party-in-interest. App. Br. 2.

SUMMARY

Appellant files this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 1–33, 44, and 45 as unpatentable under 35 U.S.C. § 101 as being directed to nonstatutory subject matter.

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellant's claimed invention is directed to methods and associated apparatus involving designing a ligand, *ab initio*, that will bind to a binding site of a macromolecular target, or of identifying a modification to a ligand for improving the affinity of the ligand to a binding site of a macromolecular target. Abstr.

REPRESENTATIVE CLAIM

Claim 1 is representative of the claims on appeal and recites:

1. A method for identifying a ligand that binds to a binding site of a macromolecular target, the method comprising:
 - a) identifying a target list of atoms forming the surface of the target binding site, each atom in the target list being referred to hereinafter as a target theta atom;
 - b) classifying the target theta atoms according to atom type, the atom type of each target theta atom being referred to hereinafter as the target theta atom type and being selected from a predetermined list of possible theta atom types;
 - c) extracting from a structural database of biological macromolecules, information about non-bonding, intra-molecular or inter-molecular atom to atom contacts, where

the atom type of a first atom in a contacting pair of atoms, hereinafter referred to as a reference theta atom, is one of the predetermined list of possible theta atom types and the atom type of the opposing, second atom of the pair, hereinafter referred to as a reference iota atom, is one of a predetermined list of possible iota atom types, said information comprising spatial and/or contextual data about the reference iota atom relative to the reference theta atom, and said data collected for a plurality of contacts involving a reference theta atom of the same theta atom type from the said database is hereinafter referred to as a theta contact set;

- d) for each target theta atom identified in the target list in b), superimposing in or around the target binding site data relating to a given iota atom type, or a predetermined group of related iota atom types, from the corresponding theta contact set extracted in c);
- e) combining and/or parsing the superimposed data in such a way as to predict one or more favoured regions of the binding site where the given iota atom type, or the predetermined group of related iota atom types, has high theoretical propensity to be located; and
- f) with a candidate ligand notionally docked into the binding site, comparing the type and position of one or more of the atoms of the candidate ligand with the predicted favoured regions for the respective iota atom types, to identify a modification to the candidate ligand, in terms of alternate and/or additional candidate ligand atoms, that will produce a greater intersection between the alternate and/or additional candidate ligand atoms and the respective iota atom type favoured regions, leading to an improvement in the affinity of the modified candidate ligand to the binding site compared to the unmodified candidate ligand;

wherein each non-bonding intra-molecular or inter-molecular contact in the database is defined as a contact between

opposing residues of a protein fold or between opposing monomer units of a macromolecular fold or between two interacting macromolecular partners and is specifically between a reference theta atom on one side of the fold or first interacting partner and a reference iota atom on the opposing side or second interacting partner; in an instance where the following condition is satisfied:

$s - R_w \leq t$, wherein s is the separation between the two atoms of the contact, R_w is the sum of the van de Waals radii of the two atoms of the contact, and t is a predetermined threshold distance; and

wherein the classification by target theta atom type in b) is unique such that there is no intersection between the data of a theta contact set extracted in c) for a given theta atom type and the data of any other theta contact set extracted in c) for any other theta atom type, apart from data concerning contacts involving the given theta atom as the iota atom.

App. Br. 23.

ISSUES AND ANALYSES

We agree with, and adopt, the Examiner's findings, reasoning, and conclusion that the claims on appeal are directed to nonstatutory subject matter. We address the arguments raised by Appellant below.

Issue

Appellant argues that the Examiner erred in concluding that the claims are directed to a judicial exception to Section 101, *viz.*, an abstract idea.

App. Br. 4.

Analysis

The Examiner finds that the claims recite a method including the steps of extracting and categorizing information, combining theoretical information, comparing it with docking information of a ligand, and making conclusions about possible changes in ligand structure. Final Act. 3. The Examiner finds that all of these concepts relate to organization, processing, comparing and deducing information, which can be performed mentally and is an idea of itself. *Id.* Therefore, concludes the Examiner, the claims are directed to an abstract idea, which is a judicial exception to Section 101. *Id.*

Appellant argues that the claims are directed to a method of identifying a ligand that binds to a macromolecular target by computationally quantifying and comparing various interactions between a candidate ligand molecule and its putative macromolecular target to identify modifications in the candidate ligand that will produce a greater affinity of the modified candidate ligand for the macromolecular binding site compared to the unmodified candidate ligand. App. Br. 4. Appellant asserts that the method thereby identifies a ligand with enhanced affinity for the macromolecular target. *Id.* According to Appellant, the method is a new and non-obvious alternative to time consuming wet chemistry techniques involving mutating candidate therapeutic molecules and testing their binding to the macromolecular target, particularly because many different mutations are generally required. *Id.* (citing Spec. 2).

Appellant argues that, because the claims are directed to an improvement to another technology, the claims are not an abstract idea that is ineligible for patentability. App. Br. 4 (citing MPEP §§ 2106.04(a)(I), 2106.05(a)(II)). In support of this contention, Appellant points to *McRO*,

Inc. v. Bandai Namco Games Am. Inc., 837 F.3d 1299 (Fed. Cir. 2016). *Id.* at 5. Appellant argues that the claims on appeal are analogous to those at issue in *McRO*, in which the court considered the patent eligibility of “[a] method for automatically animating lip synchronization and facial expression of three-dimensional characters.” *Id.* (quoting *McRO*, 837 F.3d at 1307).

Appellant argues that in *McRO*, the claimed method comprised a series of computational steps that generated a “final stream of output morph weight sets” that was subsequently applied “to a sequence of animated characters to produce lip synchronization and facial expression control of said animated characters.” App. Br. 5 (quoting *McRO*, 837 F.3d at 1308). Appellant asserts that, in upholding the patentability of the *McRO* claims, our reviewing court held that: “The claimed process uses a combined order of specific rules that renders information into a specific format that is then used and applied to create desired results: a sequence of synchronized, animated characters.” *Id.* (quoting *McRO*, 837 F.3d at 1315).

Appellant also points to the Board’s prior decision in *Ex Parte Hakkani-Tur*, Appeal No. 2017-010766, 2018 WL 2335121 (PTAB May 10, 2018). Appellant argues that the claims in *Hakkani-Tur* were directed to a system that trained a spoken language understanding (SLU) classifier that made use of a corpus of user utterances, then semantically parsed the utterances and produced a parse graph representing all user utterances. App. Br. 5. According to Appellant, the user utterances graph was then clustered into intent-wise homogeneous groups of user utterances that were then used to train the SLU classifier. *Id.* Appellant quotes the Board’s conclusion that: “The utterance intent clustering limitation, which produces intent-wise

homogeneous groups that are then used to train the SLU classifier, is improving a technological process, as it is improving a specific process by which an SLU classifier is trained,” and that the claims were therefore directed to patent-eligible subject matter. *Id.* (quoting *Hakkani-Tur* at 8).

Appellant contends that the claimed method analogously uses a combined order of specific rules that renders information into a specific format that is then used and applied to create desired results: a molecule with improved target binding affinity having particular modified structural elements. App. Br. 5. Furthermore, argues Appellant, the claims do not merely organize information into a new form, but rather go beyond rendering the information into a new format used to create the desired result. *Id.* at 6. Appellant asserts that, as in *Hakkani-Tur*, the presently claimed method generates new information. *Id.*

Furthermore, asserts Appellant, the claims are also patent-eligible because they recite an inventive concept, improving upon the laborious wet-chemistry process of generating and testing mutant binding molecules and thereby amounting to significantly more than merely reciting abstract ideas. App. Br. 6 (citing *Mayo Collaborative Servcs v. Prometheus Labs., Inc.*, 566 U.S. 66, 72–73 (2012) (holding that claims are patent eligible when they “contain other elements or a combination of elements, sometimes referred to as an ‘inventive concept,’ sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself”)).

Appellant disputes the Examiner’s finding that the claims recite: “steps of extracting and categorizing information, combining theoretical information, comparing it with docking information of a ligand, and making

conclusions about possible changes in ligand structure” and the Examiner’s conclusion that: “[a]ll of these concepts relate to organization, processing, comparing and deducing information, which can be performed mentally and is an idea of itself.” App. Br. 6 (quoting Final Act. 3). To the contrary, asserts Appellant, the claims are not directed merely to the concepts of organization, processing, comparing, and deducing information, but instead recite a limited, very specific set of rules, something the Federal Circuit considered such an important distinction in *McRO*. *Id.* (citing *McRO*, 837 F.3d at 1316; also citing MPEP § 2106.04(a)(I)). Similarly, argues Appellant, the claims on appeal produce a technological improvement that results in a concrete, tangible thing (a molecule with improved target binding affinity) and are therefore not directed to merely an abstract idea. *Id.* at 7.

We do not find Appellant’s arguments persuasive. In performing an analysis of patentability under Section 101, we follow the framework set forth by the Supreme Court in *Mayo*. We are also mindful of, and guided by, the United States Patent and Trademark Office’s 2019 Revised Patent Subject Matter Eligibility Guidance, 84(4) Fed. Reg. 50–57 (January 7, 2019) (the “2019 Guidance”).

Appellant’s claim 1 recites: “A method for identifying a ligand that binds to a binding site of a macromolecular target...” Following the first step of the *Mayo* analysis, we find that the claims are directed to a process, or method, and therefore fall into one of the broad statutory categories of patent-eligible subject matter under 35 U.S.C. § 101.

In the next step of the *Mayo* analysis, we determine whether the claims at issue are directed to a nonstatutory, patent-ineligible concept, i.e., a

law of nature, a phenomenon of nature, or an abstract idea. *Mayo*, 566 U.S. at 70–71. If the claims are so directed, we next consider the elements of each claim both individually and “as an ordered combination” to determine whether additional elements “transform the nature of the claim” into a patent-eligible application. *Id.* at 78–79; *see also Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015). Specifically, the Supreme Court considered this second step as determining whether the claims recite an element or combination of elements that is “sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.” *Mayo*, 566 U.S. at 72–73. More specifically, in this second step of the *Mayo* analysis, we look to whether the claim recites one of the judicially-created exceptions to Section 101, i.e., an abstract idea, a law of nature, or a natural phenomenon. *See* 2019 Guidance 54 (step 2A, prong 1).

If we determine that the claim recites a judicial exception, we then determine whether the limitations of the claim reciting the judicial exception are integrated into a practical application. *Id.* (Step 2A, Prong 2).

Finally, if we determine that the claim is directed to a judicially-created exception to Section 101, we evaluate the claim under the next step of the *Mayo* analysis, considering the elements of each claim both individually and “as an ordered combination” to determine whether additional elements “transform the nature of the claim” into a patent-eligible application. *Mayo*, 566 U.S. at 78–79; 2019 Guidance at 56 (Step 2B).

Claim 1 is directed to: “A method for identifying a ligand that binds to a binding site of a macromolecular target” and recites the following steps:
(1) identifying a target list of atoms forming the surface of the target binding

site (i.e., target theta atoms) (step a); (2) classifying the target theta atoms according to atom type (step b); (3) extracting from a database information about non-bonding, intra-molecular or inter-molecular atom-to-atom contacts between target theta atoms and other atoms (i.e., iota atoms) (step c); (4) for each identified target theta atom, superimposing in or around the target binding site data relating to a given iota atom type (step d); (5) combining and/or parsing the superimposed data in such a way as to predict one or more favored regions of the binding site where the given iota atom type has a high theoretical propensity to be located (step e); (6) modeling binding of the ligand to the binding site, and comparing the type and position of one or more of the atoms of the candidate ligand with the predicted favored regions for the respective iota atom types, to identify a modification to the candidate ligand, leading to an improvement in the affinity of the modified candidate ligand to the binding site compared to the unmodified candidate ligand (step f); (7) and subject to certain conditions (remaining limitations)).

Put more succinctly, the claims are directed to a computer-based method of modeling how the atomic structure of an existing or candidate ligand can be modified to improve binding of the ligand at a binding site on a target protein, using information derived from a database of information about non-bonding, intra-molecular or inter-molecular atom-to-atom contacts. *See Spec. 1, 3–4.*

All of the steps (1)–(6) recite procedures that are essentially computational in nature in that they involve extracting information from a database concerning atomic interactions in a ligand-binding site complex and predicting the interactions that will yield advantageous ligand binding.

See Spec. 1. Furthermore, all of the steps recited in the claims may be performed on a general-purpose computer. *See* Spec. 21 (“In an embodiment, the method of identifying a modification to a candidate ligand is a computer-implemented method. In an embodiment, any one or more of the steps S1-S7 [i.e., steps (1)-(7) *supra*] is/are performed on a computer”); *see also* Spec. Fig. 7.

Because the steps recited in the claim require nothing more than the identification, comparison, and manipulation of data (values) in a general purpose computer, we agree with the Examiner that the claims are directed to an abstract idea, of the sort that could be performed mentally. That is, a person, armed with paper and pencil, could perform the steps of comparing known target atoms to a database of atom-to-atom interactions and using that information to design an advantageous design for a ligand binding site. Any such abstract idea, when coupled to a generic computer performing functions that are within the regular repertoire of computer functions, are not patent eligible. *See CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1371 (Fed. Cir. 2011) (citing *Parker v. Flook*, 437 U.S. 584, 586 (1978)); *see also CyberSource*, 654 F.3d at 1372–73.

Appellant argues that the claims are not directed to an abstract idea, because the claims are directed to an improvement to another technology *See* App. Br. 5–6 (citing *McRO*, 837 F.3d at 1307). We disagree. The analysis in *McRO* expressly looked to “whether the claims in these patents focus on a specific means or method that improves the relevant technology [in that case, vocal synchronization of animated characters] or are instead directed to a result or effect that itself is the abstract idea and merely invoke generic processes and machinery.” *McRO*, 837 F.3d at 1314. In the appeal

before us, the abstract idea of optimizing ligand binding by designing a binding site that advantageously selects atomic interactions from a stored basis is “directed to a result or effect that itself is the abstract idea and merely invoke generic processes and machinery.” *Id.*

Furthermore, “[i]n cases involving software innovations, th[e] inquiry often turns on whether the claims focus on ‘the specific asserted improvement *in computer capabilities* . . . or, instead, on a process that qualifies as an ‘abstract idea’ for which computers are invoked merely as a tool.” *Finjan, Inc. v. Blue Coat Sys., Inc.*, 879 F.3d 1299, 1303 (Fed. Cir. 2018) (emphasis added) (quoting *Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1335–36 (Fed. Cir. 2016) (internal quotation marks omitted)).

Appellant’s claims are not directed to the improvement of a computer-based technology, as in *McRO*, but rather use a general-purpose computer as a tool for calculating the maximally advantageous atomic design for a ligand binding site. As such, we conclude that the claims are directed to a judicial exception to Section 101, i.e., an abstract idea. (Step 2A, prong 1).

Having determined that the claims are directed to an abstract idea, we next look to see whether the claims are integrated into a practical application. 2019 Guidance 54 (step 2A, prong 2). The Guidance provides additional context for this analysis, stating that: “A claim that integrates a judicial exception into a practical application will apply, rely on, or use the judicial exception in a manner that imposes a meaningful limit on the judicial exception, such that the claim is more than a drafting effort designed to monopolize the judicial exception.” *Id.* at 53.

In the present case, we find that the claims recite no additional steps other than the abstract idea, as implemented on a general-purpose computer,

that would constitute integration into a practical application. As such, we find that the claims do not impose meaningful limits upon the abstract idea recited in the claims. For the same reason, we find that, considering the elements of each claim both individually and “as an ordered combination” the claims recite no additional elements or steps that would suffice to “transform the nature of the claim” into a patent-eligible application. *Mayo*, 566 U.S. at 78–79; 2019 Guidance at 56 (Step 2B).

We therefore conclude that the claims are directed to nonstatutory subject matter, and we affirm the Examiner’s rejection of the claims.

CONCLUSION

The Examiner’s rejection of claims 1–33, 44, and 45 under 35 U.S.C. § 101 is affirmed.

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

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1–33, 44, 45	101	Nonstatutory subject matter	1–33, 44, 45	
Overall Outcome			1–33, 44, 45	