EXHIBIT 21

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re U.S. Patent of:		§	
	John Bridgham, et al.	§	Examiner: Unknown
Patent No.:	6,654,505 B2	§	Group Art Unit: Unknown
Issued:	November 25, 2003	§	Appl. No. Unknown
For:	SYSTEM AND APPARATUS FOR SEQUENTIAL PROCESSING OF ANALYTES	§	Atty Docket No.: INV850/36024

MAIL STOP *INTER PARTES* REEXAM
ATTN: Central Reexamination Unit
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

REQUEST FOR INTER PARTES REEXAMINATION OF U.S. PATENT NO. 6,654,505 B2

Dear Sir:

Pursuant to 37 C.F.R. § 1.915(b)(8), the Real Party in Interest, Life Technologies Corporation ("Requester"), hereby respectfully requests reexamination pursuant to 35 U.S.C. §§ 311 *et seq.* and 37 C.F.R. §§ 1.902 *et seq.* of Claims 1-6 of U.S. Patent No. 6,654,505 ("the '505 patent") (Exhibit PAT-A) filed July 17, 2001 and issued November 25, 2003 to Bridgham *et al.* The '505 patent was originally examined by Examiner Yon J. Couso.

Requester informs the Examiner that the '505 patent is involved in litigation in the United States District Court for the District of Delaware, No. 1:09-cv-00706-RK.

In accordance with 37 C.F.R. § 1.915(a) and pursuant to 37 C.F.R. § 1.20(c)(2), the Commissioner is authorized to deduct a fee of $8,800 from VINSON & ELKINS L.L.P. Deposit Account Number 22-0365/INV850-36024. If additional fees are due or if an overpayment has been made, the Commissioner is authorized to deduct or credit the proper amount to VINSON & ELKINS L.L.P. Deposit Account Number 22-0365/INV850-36024.

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5. Wilson *et al.*, J. Cell Science, 109:2101-2109 (1996) ("Wilson") Anticipates Claim 1 and Renders Obvious the Claims of the '505 Patent 20

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1. Substantial new question of patentability 26: Claims 1-3 of the '505 patent are obvious over the '150 patent in view of the '014 publication under 35 U.S.C. § 103 124

2. Substantial new question of patentability 27: Claims 1-3 of the '505 patent are obvious over the '150 patent in view of the '611 publication under 35 U.S.C. § 103 128

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1. Substantial new question of patentability 36: Claims 1-6 of the '505 patent are obvious over Schmidt in view of the '014 publication under 35 U.S.C. § 103 161

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5. Substantial new question of patentability 40: Claims 1-6 of the '505 patent are obvious over Schmidt in view of the '405 patent and the '611 publication under 35 U.S.C. § 103 180

6. Substantial new question of patentability 41: Claims 1-6 of the '505 patent are obvious over Schmidt in view of the '396 patent under 35 U.S.C. § 103 186

7. Substantial new question of patentability 42: Claims 1-6 of the '505 patent are obvious over Schmidt in view of Gelles under 35 U.S.C. § 103 190

8. Substantial new question of patentability 43: Claims 1-6 of the '505 patent are obvious over Schmidt in view of the '764 patent under 35 U.S.C. § 103 195

9. Substantial new question of patentability 44: Claims 1-6 of the '505 patent are obvious over Schmidt in view of DiMilla under 35 U.S.C. § 103 200

10. Substantial new question of patentability 45: Claims 1-6 of the '505 patent are obvious over Schmidt in view of NIH Image under 35 U.S.C. § 103 204

L. Substantial new questions of patentability 46-53: Claims 1-6 of the '505 patent are obvious over Wilson under 35 U.S.C. § 103 208

1. Substantial new question of patentability 46: Claim 1 of the '505 patent is obvious over Wilson in view of the '014 publication under 35 U.S.C. § 103 208

2. Substantial new question of patentability 47: Claim 1 of the '505 patent is obvious over Wilson in view of the '611 publication under 35 U.S.C. § 103 211

3. Substantial new question of patentability 48: Claims 1-6 of the '505 patent are obvious over Wilson in view of the '405 patent under 35 U.S.C. § 103 214

4. Substantial new question of patentability 49: Claims 1-6 of the '505 patent are obvious over Wilson in view of the '405 patent and the '611 publication under 35 U.S.C. § 103 218

5. Substantial new question of patentability 50: Claims 1-6 of the '505 patent are obvious over Wilson in view of Gelles under 35 U.S.C. § 103 223

6. Substantial new question of patentability 51: Claims 1-6 of the '505 patent are obvious over Wilson in view of the '764 patent under 35 U.S.C. § 103 227

7. Substantial new question of patentability 52: Claims 1-2 of the '505 patent are obvious over Wilson in view of DiMilla under 35 U.S.C. § 103 231

8. Substantial new question of patentability 53: Claims 1-3 of the '505 patent are obvious over Wilson in view of NIH Image under 35 U.S.C. § 103 233

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1. Substantial new question of patentability 54: Claims 1-4 of the '505 patent are obvious over Dow in view of the '014 publication under 35 U.S.C. § 103 236

2. Substantial new question of patentability 55: Claims 1-4 of the '505 patent are obvious over Dow in view of the '611 publication under 35 U.S.C. § 103 240

3. Substantial new question of patentability 56: Claims 1-6 of the '505 patent are obvious over Dow in view of the '405 patent under 35 U.S.C. § 103 243

4. Substantial new question of patentability 57: Claims 1-6 of the '505 patent are obvious over Dow in view of the '405 patent and the '611 publication under 35 U.S.C. § 103 247

5. Substantial new question of patentability 58: Claims 1-4 of the '505 patent are obvious over Dow in view of the '396 patent under 35 U.S.C. § 103 252

6. Substantial new question of patentability 59: Claims 1-6 of the '505 patent are obvious over Dow in view of Gelles under 35 U.S.C. § 103 255

7. Substantial new question of patentability 60: Claims 1-6 of the '505 patent are obvious over Dow in view of the '182 patent under 35 U.S.C. § 103 259

8. Substantial new question of patentability 61: Claims 1-6 of the '505 patent are obvious over Dow in view of the '764 patent under 35 U.S.C. § 103 263

9. Substantial new question of patentability 62: Claims 1-4 of the '505 patent are obvious over Dow in view of DiMilla under 35 U.S.C. § 103 266

10. Substantial new question of patentability 63: Claims 1-4 of the '505 patent are obvious over Dow in view of NIH Image under 35 U.S.C. § 103 269

N. Substantial new questions of patentability 64-67: Claims 1-6 of the '505 patent are obvious over NIH Image under 35 U.S.C. § 103 272

1. Substantial new question of patentability 64: Claims 1-3 of the '505 patent are obvious over NIH Image in view of the '611 publication under 35 U.S.C. § 103 272

2. Substantial new question of patentability 65: Claims 1-6 of the '505 patent are obvious over NIH Image in view of the '405 patent and the '611 publication under 35 U.S.C. § 103 275

3. Substantial new question of patentability 66: Claims 1-6 of the '505 patent are obvious over NIH Image in view of the '182 patent under 35 U.S.C. § 103 279

4. Substantial new question of patentability 67: Claims 1-6 of the '505 patent are obvious over NIH Image in view of the '764 patent under 35 U.S.C. § 103 283

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1. Substantial new question of patentability 68: Claims 1-6 of the '505 patent are obvious over the '405 patent in view of the '839 patent under 35 U.S.C. § 103 286

2. Substantial new question of patentability 69: Claims 1-6 of the '505 patent are obvious over the '405 patent in view of the '611 publication under 35 U.S.C. § 103 290

3. Substantial new question of patentability 70: Claims 1-6 of the '505 patent are obvious over the '405 patent in view of DiMilla under 35 U.S.C. § 103 293

4. Substantial new question of patentability 71: Claims 1-6 of the '505 patent are obvious over the '405 patent in view of the '182 patent under 35 U.S.C. § 103 297

5. Substantial new question of patentability 72: Claims 1-6 of the '505 patent are obvious over the '405 patent in view of the '764 patent under 35 U.S.C. § 103 301

P. Substantial new questions of patentability 73-75: Claims 1-6 of the '505 patent are obvious over the '611 publication under 35 U.S.C. § 103 305

1. Substantial new question of patentability 73: Claims 1-4 of the '505 patent are obvious over the '611 publication in view of the '839 patent under 35 U.S.C. § 103 305

2. Substantial new question of patentability 74: Claims 1-2 of the '505 patent are obvious over the '611 publication in view of DiMilla under 35 U.S.C. § 103 308

3. Substantial new question of patentability 75: Claims 1-6 of the '505 patent are obvious over the '611 publication in view of the '182 patent under 35 U.S.C. § 103 310

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VI. CONCLUSION

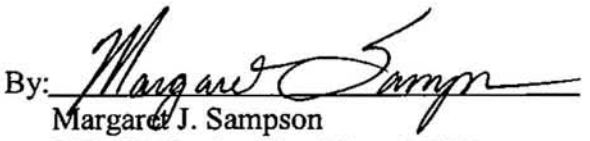
The prior art documents presented in the above Request were either not previously considered by the Office or are now being presented in a new light pursuant to MPEP § 2642(II)(A). Claims 1-6 of the '505 patent are not patentable over the prior art documents cited herein. The prior art documents teach the subject matter of the '505 patent in a manner such that substantial new questions of patentability for all claims are raised by this Request.

In view of the foregoing, it is respectfully submitted that a substantial new question of patentability of Claims 1-6 of U.S. Patent No. 6,654,505 has been raised by this Request. Accordingly, the Office is requested to grant this request and to initiate reexamination with special dispatch.

As an aid to the application to the presented prior art to the claims of the '505 patent, corresponding claim charts are provided at Exhibits CC-A through CC-P-3 attached hereto.

Date: December 31, 2009

Respectfully submitted,

By: 

Margaret J. Sampson
USPTO Registration No.: 47,052
Attorney for Requester

EXHIBIT 22

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
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MAR 23 2010

CENTRAL REEXAMINATION UNIT

EX PARTE REEXAMINATION COMMUNICATION TRANSMITTAL FORM

REEXAMINATION CONTROL NO. *95/001,292*.

PATENT NO. *6,654,505 B2 ET*.

ART UNIT *3991*.

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above identified *ex parte* reexamination proceeding (37 CFR 1.550(f)).

Where this copy is supplied after the reply by requester, 37 CFR 1.535, or the time for filing a reply has passed, no submission on behalf of the *ex parte* reexamination requester will be acknowledged or considered (37 CFR 1.550(g)).



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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO.
95/001,292	12/31/2009	6,654,505 B2	INV850/4-046REUS	9037

22918 7590 03/23/2010

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EXAMINER	
BRUMBACK, BRENDA G	
ART UNIT	PAPER NUMBER
3991	

MAIL DATE	DELIVERY MODE
03/23/2010	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.

ORDER GRANTING/DENYING REQUEST FOR* INTER PARTES *REEXAMINATION	**Control No.**	**Patent Under Reexamination**	
	95/001,292	6,654,505 B2 ET AL.	
	Examiner	**Art Unit**	
	BRENDA BRUMBACK	3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

The request for *inter partes* reexamination has been considered. Identification of the claims, the references relied on, and the rationale supporting the determination are attached.

Attachment(s): ☐ PTO-892 ☒ PTO/SB/08 ☐ Other: _____

1. ☒ The request for *inter partes* reexamination is GRANTED.

☐ An Office action is attached with this order.

☒ An Office action will follow in due course.

2. ☐ The request for *inter partes* reexamination is DENIED.

This decision is not appealable. 35 U.S.C. 312(c). Requester may seek review of a denial by petition to the Director of the USPTO within ONE MONTH from the mailing date hereof. 37 CFR 1.927. EXTENSIONS OF TIME ONLY UNDER 37 CFR 1.183. In due course, a refund under 37 CFR 1.26(c) will be made to requester.

All correspondence relating to this *inter partes* reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of this Order.

Transmittal of Communication to Third Party Requester Inter Partes Reexamination	Control No.	Patent Under Reexamination	
	95/001,292	6,654,505 B2 ET AL.	
	Examiner	Art Unit	
	BRENDA BRUMBACK	3991	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address. --

Enclosed is a copy of the latest communication from the United States Patent and Trademark Office in the above-identified reexamination proceeding. 37 CFR 1.903.

Prior to the filing of a Notice of Appeal, each time the patent owner responds to this communication, the third party requester of the *inter partes* reexamination may once file written comments within a period of 30 days from the date of service of the patent owner's response. This 30-day time period is statutory (35 U.S.C. 314(b)(2)), and, as such, it cannot be extended. See also 37 CFR 1.947.

If an *ex parte* reexamination has been merged with the *inter partes* reexamination, no responsive submission by any *ex parte* third party requester is permitted.

All correspondence relating to this inter partes reexamination proceeding should be directed to the **Central Reexamination Unit** at the mail, FAX, or hand-carry addresses given at the end of the communication enclosed with this transmittal.

Inter Partes Reexamination

Procedural Posture

The Third Party request filed on 12/31/09 for *inter partes* reexamination of claims 1-6 of United States Patent Number 6,654,505 to Bridgham *et al.* is acknowledged. The reexamination of U.S. Patent No. 6,654,505 is assigned control number 95/001,292.

Decision on Reexamination Request

A substantial new question of patentability affecting claims 1-6 of United States Patent Number 6,654,505 is raised by the present request for *inter partes* reexamination.

Status of Claims

Claims 1-6 are present in the 6,654,505 patent.

Claims 1-6 are currently subject to reexamination proceedings

Information Disclosure Statement

The Information disclosure statement filed on 12/31/09 by Third Party Requester has been considered. A signed copy of the PTO/SB/08a form is attached hereto.

Priority

US Patent 6,654,505 issued from US Application 09/907,795, filed on 07/17/01;

which is a Division of application No. 09/424,028, filed as application No. PCT/US/11224 on 5/22/98;

which is a continuation-in-part of application No. 08/862,610, filed on 05/23/97, now abandoned.

Third Party Requester alleges at pages 7-8 of the Request that although the '505 patent claims a priority date of May 23, 1997, the claimed chain of priority prior to the PCT application is invalid. The '028 and PCT applications each claim priority to U.S. Appl. Ser. No. 08/862,610 ("the '610 application"), which was filed on May 23, 1997. Requester asserts that the '610 application was expressly abandoned on March 11, 1998, in favor of U.S. Appl. Ser. No. 08/946,138, which was filed on October 7, 1997, and which claims priority to the '610 application. Requester asserts that because the '610 application was not pending at the time the PCT application was filed, the priority claim of the PCT and '028 applications to the '610 application is invalid. A review of the 08/862,610 application confirms an express abandonment of 08/862,610 on 03/11/1998 in favor of 08/946,138. Therefore, the '610 application was not pending at the time of the PCT application and **the priority date of the '505 patent is determined to be 05/22/1998**.

The '505 Patented Claims

The '505 patent consists of claims 1-6 drawn to a device-readable medium embodying a program to generate images of a planar array of microparticles and track positions of the microparticles during processing steps.

Claim 1 is representative.

1. A device-readable medium embodying a program of instructions for execution by said device to perform a method of generating images of a planar array of microparticles and tracking positions of the microparticles during a sequence of processing steps, said program of instructions comprising instructions for:

rendering a plurality of digital images of the planar array of the microparticles during the sequence of processing steps, based on optical signals generated at the microparticles; and

processing the plurality of digital images, wherein said processing includes correlating the optical signals generated at each microparticle with its corresponding image in each of the plurality of digital images.

Documents Cited in the Request as Raising an SNQ

WO 96/12014, 04/25/1996 to Brenner (hereinafter, "Brenner").

Gelles *et al. Tracking kinesin-driven movements with nanometer-scale precision.* Nature, 331:450-453 (1988) (hereinafter, "Gelles").

U.S. Patent No. 6,057,150 issued 05/02/2000 to Lee *et al.* (hereinafter "Lee").

Schmidt *et al. Integrin-Cytoskeletal Interactions in Migrating Fibroblasts are Dynamic, Asymmetric, and Regulated.* J. Cell Biology, 123(4):977-991 (1993) (hereinafter, "Schmidt").

Wilson *et al. Single particle tracking of cell-surface HLA-DR molecules using R-phycoerythrin labeled monoclonal antibodies and fluorescent digital imaging.* J.Cell Science, 109:2101-2109 (1996) (hereinafter "Wilson").

Dow *et al. A simple microcomputer-based system for real-time analysis of cell behaviour.* J. Cell Science, 87:171-182 (1987) (hereinafter "Dow").

NIH Image Version 1.58 Manual 1995 (hereinafter, "NIH").

Wernet *et al. Particle displacement tracking technique and Cramer-Rao lower bound error in centroid estimates from CCD imagery.* Experiments in Fluids, 15:295-307 (1993) (hereinafter "Wernet").

U.S. Patent No. 5,415,839 issued 05/16/1995 to Zaun *et al.* (hereinafter, "Zaun").

U.S. Patent No. 5,599,668 issued 02/04/1997 to Stimpson *et al.* (hereinafter, "Stimpson").

U.S. Patent No. 5,556,764 issued 09/17/1996 to Sizto *et al.* (hereinafter, "Sizto).

WO 97/43611, 11/20/1997 to Stern (hereinafter, "Stern").

U.S. Patent No. 6,151,405 issued 11/21/2000 to Douglass *et al.* (hereinafter "Douglass").

DiMilla *et al. Maximal Migration of Human Smooth Muscle Cells on Fibronectin and Type IV collagen Occurs at an Intermediate Attachment Strength.* J. Cell Biology, 122(3):729-737 (1993) (hereinafter "DiMilla").

U.S. Patent No. 5,257,182 issued 10/26/0993 to Luck et al. (hereinafter "Luck").

U.S. Patent No. 6,122,396 issued 09/19/2000 to King et al. (hereinafter "King").

Substantial New Question of Patentability

For "a substantial new question of patentability" to be present, it is only necessary that:

A. The prior art patents and/or printed publications raise a substantial question of patentability regarding at least one claim i.e. the prior art teaching is such that there is a substantial likelihood that a reasonable examiner would consider the teaching to be important in deciding whether or not the claim is patentable and;

B. The same question of patentability as to the claim has not been decided by the Office in a previous examination or pending reexamination of the patent or in a final holding of invalidity by the Federal Courts in a decision on the merits involving the claim.

It is not necessary that the prior art establish a *prima facie* case of unpatentability in order for a substantial new question of patentability to be present as to the claim. See MPEP 2642.

For a reexamination that was ordered on or after November 2, 2002 (the date of enactment of Public Law 107-273; see Section 13105, of the Patent and Trademark Office Authorization Act of 2002), reliance solely on old art (as the basis for a rejection) does not necessarily preclude the existence of a substantial new question of patentability (SNQ) that is based exclusively on that old art. Determinations on whether a SNQ exists in such an instance

shall be based upon a fact-specific inquiry done on a case-by-case basis. For example, an SNQ may be based solely on old art where the old art is being presented/viewed in a new light, or in a different way, as compared with its use in the earlier concluded examination(s), in view of a material new argument or interpretation presented in the request. MPEP 2642 and 2658.

1. The Third Party Requester asserts that **Brenner**, either alone or in combination with one or more of Wernet, Luck, Stimpson, Sizto, Stern, Douglass, DiMilla, Gelles, or NIH raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Brenner was neither cited nor used in a rejection in the application which issued as the `505 patent. The Brenner teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at pages 13-14 of the Request, Brenner discloses a system for scanning and tracking microparticles in a planar array, which is an automated scanning system for tracking, identifying and/or sorting classes or subpopulations of molecules through the optical detection of labeled polynucleotide tags (pages 25-27). The Brenner system provides a digital imaging device that uses a device readable medium to detect, capture and analyze images of a planar array of microparticle-polynucleotide conjugates bound to optically labeled (*e.g.*, fluorescent) target molecules. Brenner discloses a computer and video output to capture and analyze digital images of fluorescent signals from individual microparticles (pages 26-27). The Brenner system also describes the analysis of a planar array of microparticles fixed to a substrate and placed on a translation table which is examined by a scanning fluorescent microscope, with photon output collected by a computer and displayed on a video (see Fig. 5 at page 26).

Brenner, either alone or in combination with one of Wernet, Luck, Stimpson, Sizto, Stern, Douglass, DiMilla, Gelles, or NIH raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Brenner teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Brenner, either alone or in combination with one of Wernet, Luck, Stimpson, Sizto, Stern, Douglass, DiMilla, Gelles, or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

2. The Third Party Requester asserts that **Gelles**, either alone or in combination with one or more of Stern, Douglass, King, Luck, Sizto, DiMilla or NIH raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Gelles was neither cited nor used in a rejection in the application which issued as the `505 patent. The Gelles teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As set forth at pages 15-17 of the Request, Gelles discloses a method of generating images and optically tracking individual microparticles (latex beads) which are positioned on a glass coverslip in a planar array (pages 450-451). Gelles teaches a digital image analysis system that allows a user to optically track the movements of a planar array of kinesin coated microparticles over time as they interact with a layer of microtubules. The Gelles system provides a digital imaging device comprising a device readable medium to detect, capture and analyze images of microspheres obtained through video-enhanced differential interference contrast microscopy. Gelles teaches calculation of the centroid of individual beads based on an

analysis of pixel assignments within captured digital images (page 450). Gelles teaches analyzing a kernel consisting of a single bead image in which a plurality of pixels is assigned to the kernel image. Gelles teaches using the pixel information for such a kernel to analyze the position of other beads within a plurality of digital images based on the pixels assigned to each such bead within the digital image. The digital image of a single bead is used to generate a data set that includes the number of pixels encompassed by the single bead as well as the measured intensity level for each such pixel. This kernel data set is then used in a cross-correlation analysis as a template to search for, and identify other areas (*i.e.*, beads) within the acquired digital images where the pixel intensity distributions most closely match that of the kernel.

Gelles, either alone or in combination with one of Stern, Douglass, King, Luck, Sizto, DiMilla or NIH raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Gelles teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Gelles, either alone or in combination with one of Stern, Douglass, King, Luck, Sizto, DiMilla or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

3. The Third Party Requester asserts that **Lee**, either alone or in combination with one or more of Brenner, Stern, Douglass, King, Gelles, Luck, Sizto, DiMilla or NIH raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Lee was neither cited nor used in a rejection in the application which issued as the `505 patent. The Lee teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

Lee discloses a system for generating images and tracking the positions of microspheres on a cell membrane in a substantially planar array (col. 9-10). Lee teaches a method for measuring membrane stretch by using fluorescently labeled microspheres as fiducial markers. Lee's method involves placing multiple fluorescent microspheres on a membrane and then capturing and analyzing digital images of the microspheres before and after stretching of the membrane to measure positional deviations (col. 8). Lee teaches positional tracking of fluorescent signals generated at, or on, the microspheres attached to cell membranes. Lee discloses capturing video images to a computer using a device readable medium for image processing (col. 9, Fig. 11).

Lee, either alone or in combination with one of Brenner, Stern, Douglass, King, Gelles, Luck, Sizto, DiMilla or NIH raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Lee teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Lee, either alone or in combination with one of Brenner, Stern, Douglass, King, Gelles, Luck, Sizto, DiMilla or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

4. The Third Party Requester asserts that **Schmidt**, either alone or in combination with one or more of Brenner, Dow, Stern, Douglass, King, Gelles, Sizto, DiMilla, or NIH raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Schmidt was neither cited nor used in a rejection in the application which issued as the `505 patent. The Schmidt teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at page 19 or the Request, Schmidt discloses a method of generating digital images and using those digital images to track micropartieles (colloidal gold or polystyrene beads) in a planar array (page 979). Schmidt teaches a system and method for using digital images of microparticles to track adhesion receptor movements on the surface of a cell. The system disclosed by Schmidt attaches microparticles labeled with receptor specific antibodies to the surface of adherent cells. Digital images are then obtained through differential interference contrast microscopy of the microparticles, which are captured and analyzed over time to positionall track receptor movements on the cell membrane. The method taught by Schmidt employs a device readable medium to perform a cross-correlation analysis based on pixel level digital image information to track the position of microparticles being transported along a flattened adherent cell surface. Schmidt further teaches calculating the location of the positional center of individual microparticles at various points in time.

Schmidt, either alone or in combination with one or more of Brenner, Dow, Stern, Douglass, King, Gelles, Sizto, DiMilla, or NIH raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Schmidt teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Schmidt, either alone or in combination with one or more of Brenner, Dow, Stern, Douglass, King, Gelles, Sizto, DiMilla, or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

5. The Third Party Requester asserts that **Wilson,** either alone or in combination with one or more of Brenner, Stern, Douglass, Gelles, Sizto, DiMilla or NIH, raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Wilson was neither cited nor used in a rejection in the application which issued as the `505 patent. The Wilson teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at page 20 of the Request, Wilson discloses a method of generating images and tracking planar arrays of single microparticles (page 2101). Wilson teaches a method and system for using digital images to track fluorescently labeled single particles attached to HLA-DR molecules. The system disclosed in Wilson uses fluorescent microscopy to capture and analyze digital images of cells labeled with fluorescently tagged anti-HLA-DR specific antibodies in order to track particle positions on a cell surface over time (pages 2101-2103). Wilson also teaches a device readable medium to assign pixels to microparticles within the digitial images and to quantify the pixel level data with a Gaussian function (page 2103).

Wilson, either alone or in combination with one or more of Brenner, Stern, Douglass, Gelles, Sizto, DiMilla or NIH, raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Wilson teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Wilson, either alone or in combination with one or more of Brenner, Stern, Douglass, Gelles, Sizto, DiMilla or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

6. The Third Party Requester asserts that **Dow**, either alone or in combination with one or more of Brenner, Douglass, Stern, King, Gelles, Luck, Sizto, DiMilla, or NIH raises a substantial new question of patentability of claims 1-5 of the `505 Patent.

Dow was neither cited nor used in a rejection in the application which issued as the `505 patent. The Dow teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

Dow teaches a method of generating images and tracking cells in a planar array (pages 171-173). Dow discloses a system and method for tracking cell migration on extracellular matrix proteins using video-microscopy. Dow teaches capturing and analyzing sequential digital images of multiple cells as the cells migrate across extracellular matrix proteins immobilized on a glass slide. Dow describes the use of a device readable medium to perform binary filtering and implement a cell tracking algorithm (page 173). Dow further discloses calculation of the positional center of the cells being tracked.

Dow, either alone or in combination with one or more of Brenner, Douglass, Stern, King, Gelles, Luck, Sizto, DiMilla, or NIH raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Dow teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Dow, either alone or in combination with one or more of Brenner, Douglass, Stern, King, Gelles, Luck, Sizto, DiMilla, or NIH raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

7. The Third Party Requester asserts that **NIH**, either alone or in combination with one or more of Stern, Douglass, Luch or Sizto raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

NIH was neither cited nor used in a rejection in the application which issued as the `505 patent. The NIH teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As set forth on page 22 of the request, NIH discloses software-based applications that enable the generation of digital images and tracking of microparticle positions (see pagest 2, 3, 5, 35-37 and 76-77). NIH teaches analyzing objects captured in digital images and provides macros that automate digital image analysis tasks such as calculation of particle number and size within a digital image (page 35). NIH describes the use of binary and threshold filtering to measure microparticle size and position and further discloses calculation of centroids of the imaged microparticles (pages 37-38).

NIH, either alone or in combination with one or more of Stern, Douglass, Luch or Sizto raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the NIH teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, NIH, either alone or in combination with one or more of Stern, Douglass, Luch or Sizto raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

8. The Third Party Requester asserts that **Wernet**, in combination with Brenner, raises a substantial new question of patentability of claims 1-3 and 5-6 of the `505 Patent.

Wernet was neither cited nor used in a rejection in the application which issued as the `505 patent. The Wernet teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As set forth at page 23 of the request, Wernet teaches a particle displacement tracking technique and centroid calculation using images from a charge-coupled device (page 295). Wemet teaches a system and methodology for using digital images to track microparticles through calculations of individual microparticle centroid positioning. Wernet also discloses assignment of a plurality of pixels to each particle (pages 299-300).

Wernet in combination with Brenner raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Wernet teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Wernet in combination with Brenner raises a substantial new question of patentability as to claims 1-3 and 5-6, which question has not been decided in a previous examination of the `505 patent.

9. The Third Party Requester asserts that **Zaun** in combination with Douglass raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Zaun was neither cited nor used in a rejection in the application which issued as the `505 patent. The Zaun teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

Zaun teaches a system of generating images of and tracking a planar array of amplified nucleic acids (see col. 14). Zaun discloses a method and an apparatus for detecting amplified nucleic acids using a reaction/detection unit. In particular, Zaun describes a detection system

including a computer and video output (col. 27). Zaun also discloses calculation of the mean, standard deviation and range values for all pixels within a defined signal area (col. 30).

Zaun, in combination with Douglass, raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Zaun teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Zaun in combination with Douglass raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

10. The Third Party Requester asserts that **Stimpson**, in combination with Brenner, raises a substantial new question of patentability of claims 1-3 of the `505 Patent.

Stimpson was neither cited nor used in a rejection in the application which issued as the `505 patent. The Stimpson teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

Stimpson discloses a system of generating images and tracking a planar array of microparticles (see col. 22). Stimpson discloses a waveguide binding assay in which binding and dissociation can be monitored by video imaging. In particular, Stimpson describes a detection system including a charge-coupled device and computer (col. 24) and assignment of a plurality of pixels to each signal situs (col. 25).

Stimpson in combination with Brenner raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Stimpson teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Stimpson, in combination

with Brenner, raises a substantial new question of patentability as to claims 1-3, which question has not been decided in a previous examination of the `505 patent.

11. The Third Party Requester asserts that **Sizto,** in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, or Douglass raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Sizto was neither cited nor used in a rejection in the application which issued as the `505 patent. The Sizto teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at page 26 of the Request, Sizto describes a system of generating images of and tracking cells (see col. 3-4). Sizto discloses a method and an apparatus employing a device readable medium for scanning, generating images of, and classifying cells based on fluorescent data (col. 6-11). Sizto teaches determination of centroids of the cells (col. 14) and assignment of a plurality of pixels to each target cell.

Sizto, in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, or Douglass raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Sizto teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Sizto, either alone or in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, or Douglass, raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

12. The Third Party Requester asserts that **Stern** in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, Douglass, Zaun, DiMilla, or Luck raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Stern was neither cited nor used in a rejection in the application which issued as the `505 patent. The Stern teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth in the request at page 27, Stern teaches a method of scanning and tracking planar arrays of immobilized polymers (page 5). Stern discloses a system and method for detecting labeled polymers to generate highly sensitive and resolved images (page 14). Stern teaches a scanning system including a fluorescence detector or photomultiplier tube and a computer (page 20). The system taught by Stern comprises a flow cell for detecting reactions between targets and probes (page 29).

Stern in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, Douglass, Zaun, DiMilla, or Luck raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Stern teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Stern in combination with one of Gelles, Lee, Schmidt, Wilson, Dow, NIH, Douglass, Zaun, DiMilla, or Luck raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

13. The Third Party Requester asserts that **Douglass**, either alone or in combination with one or more of Brenner, Stern, Gelles, Lee, Schmidt, Wilson, Dow, NIH, Zaun, DiMilla, Luck, or Sizto, raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Douglass was neither cited nor used in a rejection in the application which issued as the `505 patent. The Douglass teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As set forth in the request at page 28, Douglass teaches a system of generating images of and tracking a planar array of cells. (col. 6-7). Douglass discloses an automated microscope system that employs a device readable medium for scanning and evaluating cellular specimens on a microscope slide. The Douglass system captures and analyzes digital images to register the location of candidate objects (cells). Douglass further describes identification of candidate objects (cells) within digital images of a planar array of microparticles based on color, size and shape characteristics and calculation of centroids of the cells (col. 8).

Douglass, either alone or in combination with one or more of Brenner, Stern, Gelles, Lee, Schmidt, Wilson, Dow, NIH, Zaun, DiMilla, Luck, or Sizto, raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Douglass teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Douglass, either alone or in combination with one or more of Brenner, Stern, Gelles, Lee, Schmidt, Wilson, Dow, NIH, Zaun, DiMilla, Luck, or Sizto raises a substantial new question of patentability as to claims 1-6 which question has not been decided in a previous examination of the `505 patent.

14. The Third Party Requester asserts that **DiMilla** in combination with one of Brenner, Gelles, Lee, Schmidt, Wilson, Dow, Douglass, or Stern raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

DiMilla was neither cited nor used in a rejection in the application which issued as the `505 patent. The DiMilla teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at page 29 of the Request, DiMilla discloses a method of generating images of and tracking planar arrays of cells (page 731). DiMilla teaches using time-lapse video microscopy of individual cell movement paths to track migration behavior. DiMilla further teaches time- lapse video microscopy and image analysis to locate and track the position of multiple cells on a planar substrate (page 733). DiMilla also discloses calculation of centroids of the cells (page 731.

DiMilla, in combination with one of Brenner, Gelles, Lee, Schmidt, Wilson, Dow, Douglass, or Stern raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the DiMilla teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, DiMilla, in combination with one of Brenner, Gelles, Lee, Schmidt, Wilson, Dow, Douglass, or Stern raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

15. The Third Party Requester asserts that **Luck** in combination with one of Brenner, Gelles, Lee, Dow, Douglass, or Stern raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

Luck was neither cited nor used in a rejection in the application which issued as the `505 patent. The Luck eachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As was set forth at page 30 of the request, Luck teaches a system of generating images of and tracking a planar array of cells (col. 3). Luck teaches classifying cells, including obtaining a sequence of images of cells of interest (col. 3-5). Luck describes determination of centroids of the cells as well as capture and display of high resolution images (col. 8).

Luck, in combination with one of Brenner, Gelles, Lee, Dow, Douglass, or Stern raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the Luck teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, Luck, in combination with one of Brenner, Gelles, Lee, Dow, Douglass, or Steraises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

16. The Third Party Requester asserts that **King** in combination with one of Gelles, Lee, Schmidt, or Dow, raises a substantial new question of patentability of claims 1-6 of the `505 Patent.

King was neither cited nor used in a rejection in the application which issued as the `505 patent. The King teachings are not considered cumulative to the references that were considered during prosecution of the `505 patent.

As set forth on page 31 of the request, King discloses a system of generating images of and tracking a planar array of microbes (col. 2-3). King discloses a microorganism-detecting apparatus that uses fluorescence microscope sections which are obtained through the function of a motor-driven xyz stage assembly (col. 2). King also discloses capturing video images to a computer for image processing,

King, in combination with one of Gelles, Lee, Schmidt, or Dow, raises an SNQ since there is substantial likelihood that a reasonable examiner would consider the King teachings to be important in deciding if one or more claims of the `505 patent are patentable. Accordingly, King in combination with one of Gelles, Lee, Schmidt, or Dow raises a substantial new question of patentability as to claims 1-6, which question has not been decided in a previous examination of the `505 patent.

Conclusion

In view of the above, the request for reexamination of claims 1-6 of U.S. Patent 6,654,505 is **GRANTED.**

A substantial new question of patentability affecting claim 1-6 of United States Patent Number 6,654,505 is raised by the present request for *inter partes* reexamination.

Duty to Disclose

The patent owner is reminded of the continuing responsibility under 37 CFR 1.985 to apprise the Office of any litigation activity, or other prior or concurrent proceeding, involving Patent No. 6,654,505 throughout the course of this reexamination proceeding. The third party requester is also reminded of the ability to similarly apprise the Office of any such activity or proceeding throughout the course of this reexamination proceeding.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT
(Not for submission under 37 CFR 1.99)

Application Number	09907795
Filing Date	2001-07-17
First Named Inventor	Bridgham, John
Art Unit	
Examiner Name	
Attorney Docket Number	INV850/36024

U.S.PATENTS

Examiner Initial*	Cite No	Patent Number	Kind Code[1]	Issue Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear
bh	1	6151405		2000-11-21	DOUGLASS et al	
	2	6122396		2000-09-19	KING et al.	
	3	6057150		2000-05-02	LEE et al	
	4	5599668		1997-02-04	STIMPSON et al.	
	5	5556764		1996-09-17	SIZTO et al	
	6	5415839		1995-05-16	ZAUN et al.	
bh	7	5257182		1993-10-26	LUCK et al.	

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U.S.PATENT APPLICATION PUBLICATIONS

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FOREIGN PATENT DOCUMENTS

Examiner Initial*	Cite No	Foreign Document Number[3]	Country Code[2]	Kind Code[4]	Publication Date	Name of Patentee or Applicant of cited Document	Pages,Columns,Lines where Relevant Passages or Relevant Figures Appear	T[5]
BB	1	WO97/43611	WO		1997-11-20	AFFYMETRIX, INC.		☐
BB	2	WO96/12014	WO		1996-04-25	LYNX THERAPEUTICS, INC.		☐

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NON-PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc), date, pages(s), volume-issue number(s), publisher, city and/or country where published.	T[5]
BB	1	DiMILLA et al., Maximal Migration of Human Smooth Muscle Cells on Fibronectin and Type IV Collagen Occurs at an Intermediate Attachment Strength, The Journal of Cell Biology, August 1993, pp. 729-737, Vol. 122, No 3, USA.	☐
↓	2	DOW et al , A simple microcomputer-based system for real-time analysis of cell behaviour, Journal of Cell Science, 1987, pp. 171-182, Vol. 87, Great Britain	☐
BB	3	GELLES et al., Tracking kinesin-driven movements with nanometre-scale precision, Nature, February 4, 1988, pp 450-453, Vol. 331, USA.	☐

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Not for submission under 37 CFR 1.99)		
	Application Number	09907795
	Filing Date	2001-07-17
	First Named Inventor	Bridgham, John
	Art Unit	
	Examiner Name	
	Attorney Docket Number	INV850/36024

bb	4	SCHMIDT et al., Integrin-Cytoskeletal Interactions in Migrating Fibroblasts are Dynamic, Asymmetric, and Regulated, The Journal of Cell Biology, November 1993, pp. 977-991, Vol. 123, No. 4, USA.	☐
	5	WERNET and PLINE, Particle displacement tracking technique and Cramer-Rao lower bound error in centroid estimates from CCD imagery, Experiments in Fluids, 1993, pp. 295-307, Vol. 15, USA.	☐
	6	WILSON et al., Single particle tracking of cell-surface HLA-DR molecules using R-phycoerythrin labeled monoclonal antibodies and fluorescence digital imaging, Journal of Cell Science, 1996, pp. 2101-2109, Vol. 109, Great Britain.	☐
bb	7	NIH Image Version 1.58 Manual.	☐
	8		☐
	9		☐

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EXAMINER SIGNATURE

Examiner Signature	Brenda Bernstock	Date Considered	2/26/10

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