EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CYTONOME/ST, LLC, Plaintiff, v. NANOCELLECT BIOMEDICAL, INC., Defendant.	)	C.A. No. 19-301 (RGA)

SUPPLEMENTAL DECLARATION OF DR. GIACOMO VACCA

I, Giacomo Vacca, Ph.D., declare the following:

1. My name is Dr. Giacomo Vacca. I have been asked to provide this supplemental declaration in response to the Declaration of Dr. Dino Carlo from February 14, 2020 (the "Di Carlo Declaration"), specifically regarding the term "pressure pulse" and how a person of skill would interpret the embodiment depicted in Figure 6 of U.S. Patent No. 9,339,850 (the "'850 Patent").

2. In summary, I disagree with Dr. Di Carlo's opinion that "[a] POSA reviewing the Asserted Patents would have understood the term 'pressure pulse' to be 'a unidirectional flow to the [microchannel/supply duct]'" because it is too narrow and technically incorrect. D.I. 67, Ex. K ¶ 91 ("Di Carlo Decl."). The claims do not say anything about directionality, and a POSA would not read them to require a particular directionality. Figure 6 is one example where the pressure pulse is *not* unidirectional and, contrary to Dr. Di Carlo's opinion, would still be operable. Figure 5 provides another example of an operable embodiment using a non-unidirectional pressure pulse. Accordingly, the embodiments depicted in these figures support that the patents are using the plain and ordinary meaning of "pressure pulse" and not a narrow meaning requiring a "unidirectional

flow." That plain and ordinary meaning, as understood by a POSA in light of the claims and specification, is "a transient wave of pressure that generally travels away from its source."

3. This declaration does not replace my January 31, 2020 declaration (D.I. 67, Ex. H, "Original Declaration"), and is made in light of the opinions in that Original Declaration. My opinions and the bases for my opinions are set forth below.

I. Analysis of Figure 6 and its "Pressure Pulse"

4. The particle sorting devices described and claimed in the asserted patents are generally aimed at "deflecting" individual "selected" particles into a desired outlet. This deflection generally involves applying a short burst of force (i.e., a "jolt") to a selected particle using a "pressure pulse," pushing the particle away from its original trajectory and onto a new trajectory. Figure 6 (reproduced below in Fig. A) illustrates one embodiment of the claimed invention,[1] in which the actuation leading to particle deflection is mediated by, e.g., a "plunger":

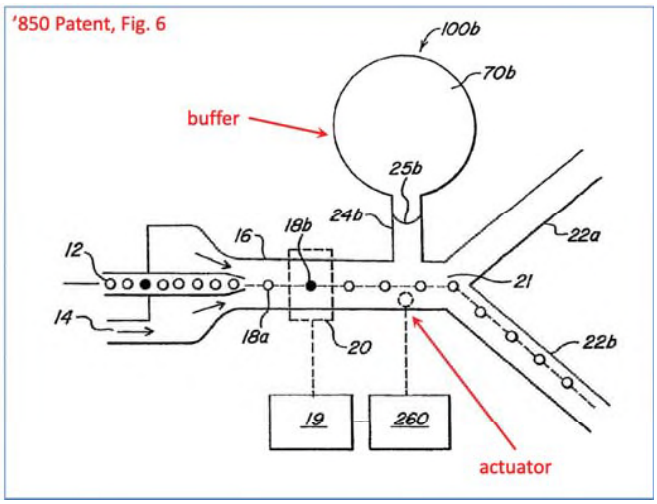


Fig. A. From Fig. 6, '850 Patent (annotated).

[1] Dr. Di Carlo is wrong to contend that Figure 6 is "a single embodiment of a single patent." Di Carlo Decl. ¶ 91. The same embodiment is depicted and described as Figure 6 in asserted U.S. Patent Nos. 10,029,263 (the "'263 Patent") and 10,029,283 (the "'283 Patent").

5. Regardless of what mechanism or technique is used to effect sorting, a necessary and critical element to sort individual particles is ***timing***. At the planned moment of actuation, a mechanism is activated, resulting in an applied force to, and in the desired deflection of, the selected particle. That application of force, by whatever mechanism (be it a pressure pulse, fluid injection, etc.), must be timed so to apply in turn to each desired particle, and must have sufficient strength to cause the necessary deflection. Many sources of variation in the system must be taken into account in order to produce a successful sort, and a properly designed, built, and operated device accounts for these variations by incorporating a certain margin in the operational parameters—an acceptable tolerance of departures from the ideal.

6. One source of variation which affects the vast majority of particle sorters is ***interparticle separation***. Generally, individual particles will pass by the sorting location on a random basis; the mathematics that describes the distribution of interparticle distances for random arrivals is called "Poisson statistics" (*see*, e.g., H. Shapiro, *Practical Flow Cytometry*, 4th ed., Wiley-Liss, 2003; p. 19–20). The fact that interparticle distances can take on a wide range of values means that, for any given average concentration of particles to be sorted, there will be a certain (calculable) fraction that come closer together than a given threshold. When this occurs, the result is a "coincidence," meaning an instance when two particles are too close together to allow sorting of one and rejection of the other. Sorting specifications, therefore, generally include that threshold, which is a trade-off between sorting accuracy and speed; and the dependence of the coincidence fraction on the particle concentration.

7. *Operability*, then, refers to the combined ability to selectively sort selected particles and to selectively not sort non-selected ones. This can be achieved if the non-selected particles are not disrupted when a selected particle is being deflected. Sorting devices that achieve the

maximum throughput (fastest flow with the closest average interparticle distance), while maintaining accuracy, are most desirable; but there can be different levels of performance among operable devices. In other words, one can choose to operate at different points on the trade-off spectrum, with different balances of performance parameters, and have acceptable results.

8. The devices of the asserted patents are no different. The goal is to sort particles, and various operable embodiments with different degrees of performance are disclosed. Specifically, these devices all operate using a "pressure pulse," and the aspects of timing and interparticle separation described above play a role. In other words, "applying a pressure pulse" to a "selected particle" ***does not imply or require that the pulse be unidirectional***. It refers to a configuration where only the particle projected to be closest to the actuator when it is triggered (plus the surrounding fluid effected by the pulse) receives a "jolt" sufficient to deflect the selected particle onto a trajectory to the sort channel. To put it another way, the claimed devices are not concerned with a "directionality" of a "flow" (as Dr. Di Carlo's interpretation suggests), but simply with establishing only ***a narrow range of jolt directions*** to effect the desired deflection. The asserted patents achieve that by combining various mechanisms of actuation with the presence of a buffer to absorb the pressure pulse. It is primarily this combination that results in a "directionality" in the claimed devices—not any intrinsic property of the pressure pulse itself.

9. These concepts are exemplified in the asserted patents. Figs. 1–4 of the '850 Patent, for example, illustrate the patents' preferred embodiment, involving two reservoirs placed opposite each other on either side of the main transport channel; one reservoir (associated with the actuator) operating as the source of the pressure pulse and the other (the buffer) acting as the absorber of the same. In this preferred embodiment, actuation of the pressure pulse is timed to coincide with the moment the selected particle passes between the two side channels leading to the reservoirs—but

the pressure pulse is not dispatched in a single direction. ***The buffer, together with the actuator, defines the narrow range of directions for the jolts that cause deflection.***

10. The annotated version of Fig. 6 below (Fig. B) demonstrates how the claimed devices need not be "unidirectional." The actuator is shown at the center of concentric half-circles (in green), which represent the pressure pulse as it expands from the actuator into the surrounding medium (the fluid in the main channel). ***The expanding pressure pulse (a type of sound wave) is substantially non-directional***, i.e., it propagates in the channel fluid as a substantially hemispherical wavefront with steadily increasing radius. The annotation shows that this expanding wave reaches more than one particle: the selected particle (filled blue circle), as well as two non-selected particles (empty blue circles). In this schematic,[2] the two non-selected particles are not so close to the selected particle to be in the narrow range of jolts that are strong enough to result in deflection; the selected particle, therefore, is the only one that ends up (correctly) getting deflected and sorted into branch 22a, ***despite the non-unidirectionality of the pressure pulse***.

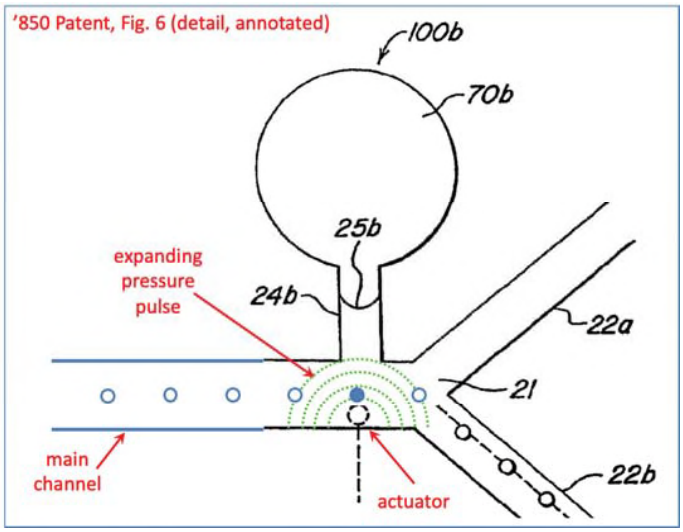


Fig. B. Detail from Fig. 6, '850 Patent (annotated).

[2] As mentioned earlier, the interparticle spacings follow a Poisson distribution, rather than the regular pattern illustrated here.

11. To be sure, there *is* a directionality to the *deflection* that occurs as a result of actuation; but that directionality is ***not inherent*** to the pressure pulse; rather, it is a consequence of the presence and location of the buffer and the side channel. Simplifying, the particle that will be deflected is the one that comes between the actuator and the side channel at the time the pressure pulse sweeps over it. The reason for that directionality in this example is that ***the buffer*** provides the pressure pulse with an "escape hatch," converting the pressure pulse into fluid motion that carries the desired particle away from a default streamline and onto a sorting streamline. So, in other words, the desired particle gets deflected in the direction that links the actuator to the side channel of the buffer. In the case above, that direction is transversal, i.e., it is substantially perpendicular to the main flow direction (as desired), due to the fact that the buffer and the actuator are directly opposite each other. It is not due to any directionality of the pressure pulse.

12. The embodiment illustrated in Fig. 6 may or may not offer the same combination of trade-offs in sorting performance as that illustrated in other embodiments, but it's certainly *operable* to sort particles. Indeed, the patentees (in the same paragraph used to describe Fig. 6; *see* '850 Patent at 9:51–56) provide some examples of how the buffer can be adjusted to adequately absorb the "pressure pulse" and cause only selected particles to receive a sufficient and appropriate jolt. In this way, the buffer is used not only to maintain operability, but possibly to achieve a performance similar to other embodiments. And just as in the preferred embodiments, in Fig. 6 the pressure pulse is *timed* to cause deflection of the selected particle at the moment the particle passes between the actuator (plunger, in this case) and the side channel.

13. The annotated reproduction of Fig. 5 from the '850 Patent below (Fig. C) illustrates yet again how the asserted patents do not require a single, fixed, directionality to the deflection of selected particles. Fig. 5 shows the actuator reservoir to the side of the non-sorting branch 22b,

while the buffer reservoir is shown to the side of the sorting branch 22a. The two reservoirs are not only not directly opposite each other, but are on separate branches of the fluidic circuit. The path between the two reservoirs is indicated as being a "low resistance path," while the rest of the non-sorting branch is indicated as being a "high resistance path." This design choice tends to concentrate the fluid displacement from the actuator to the buffer, despite the fact that that path is anything but straight. The direction which fluid disruption, caused by the pressure pulse, would take is actually ***a set of multiple directions***, indicated schematically by the purple arrows. This embodiment once again confirms a POSA's understanding that a pressure pulse, per se, does not "have a direction" or preferentially select any specific single direction; and that it is the combination of the actuator and the buffer, as constrained by the channel geometry, that governs the directions in which fluid disruption, and ultimately particle deflection, occurs.

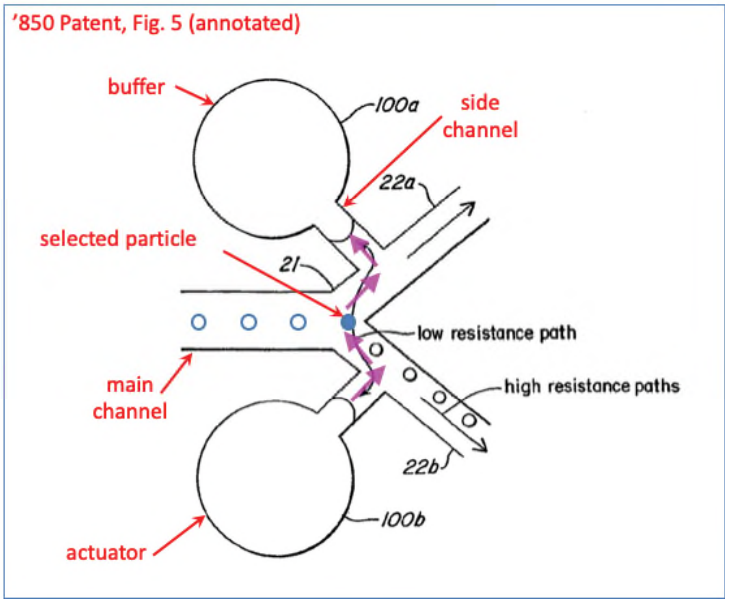


Fig. C. Detail from Fig. 5, '850 Patent (annotated).

II. Summary and Conclusion

14. In summary, a person of skill would understand that Fig. 6 of the '850 Patent is *not* unidirectional and is also *operable.* Fig. 6 therefore demonstrates that a specific directionality of

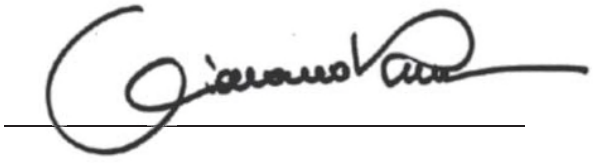
the claimed "pressure pulse" is not required (contrary to what Dr. Di Carlo contends). As shown above—specifically in Fig. B and accompanying text—"pressure pulses" can have several simultaneous "directions." The "pressure pulse" in the claims is timed precisely so as to cause the deflection of one (and, generally, only one) selected particle when that particle passes the actuator, with the buffer and the choice of timing providing the desired directionality to the deflection. Based on that, a person of skill would understand the following:

(i) To deflect only one particle at the moment it passes the actuator, a person of skill would understand that the pressure pulse must be "transient." Indeed, this is the common understanding of the word "pulse."

(ii) Furthermore, a person of skill would understand that the pressure pulse propagates in all directions away from its source, without showing a preference for one direction over another.

15. Putting this together, as used in the asserted claims, "pressure pulse" would have been understood by a person of skill at the time of the invention as "a transient wave of pressure that generally travels away from its source."

I declare, under penalty of perjury, under the laws of the United States, that the foregoing is true and correct and that this Declaration was completed this 8th day of May, 2020.



Giacomo Vacca, Ph.D.

EXHIBIT B

Langford, Melanie

From: Burrowbridge, Adam <aburrowbridge@wsgr.com>
Sent: Monday, May 11, 2020 11:17 AM
To: Moffett, Dan; Carsten, Douglas; Liston, Ian
Cc: WSGR - NanoCellect/Cytonome; NANOCELLECT (AG TEAM); Smith, Rodger (External); Raucci, Anthony D.
Subject: Re: Cytonome v. NanoCellect | Construction of "Buffer"

Dan,

Thank you for your email. We believe that it could be useful to meet and confer at 1pm ET. Particularly, we would like to discuss and consider any support from the '528 specification and, separately, the '850 specification that supports a construction broader than NanoCellect's proposal. Call in details follow:

+1-855-797-9485 US Toll free
120-32-485 Attendee access code

Best,
Adam

From: "Moffett, Dan" <dmoffett@AkinGump.com>
Date: Monday, May 11, 2020 at 11:00 AM
To: "Burrowbridge, Adam" <aburrowbridge@wsgr.com>, "Carsten, Douglas" <dcarsten@wsgr.com>, "Liston, Ian" <iliston@wsgr.com>
Cc: WSGR - NanoCellect/Cytonome <nanocellect/cytonome@wsgr.com>, "NANOCELLECT (AG TEAM)" <NANOCELLECTAGTEAM@akingump.com>, "Smith, Rodger (External)" <rsmith@mnat.com>, "Raucci, Anthony D." <araucci@MNAT.com>
Subject: RE: Cytonome v. NanoCellect | Construction of "Buffer"

[External]
Adam,

Thank you for your response. We do not agree with NanoCellect's alternative construction. The construction improperly adds a limitation that does not appear in the claims and, based on Mr. Carsten's characterization of "compressible fluid" at the *Markman* hearing (which we dispute), is essentially an effort to reassert NanoCellect's rejected 112 ¶ 6 argument that the claims should be limited to a specific embodiment in the specification.

Given the extent to which the parties have already conferred on claim construction, and "buffer" in particular, we do not believe a phone call is necessary. But we are happy to jump on a call if you believe NanoCellect can agree to a less limiting construction. Let us know.

Thank you,

Dan

Dan Moffett
AKIN GUMP STRAUSS HAUER & FELD LLP
Direct: +1 210.281.7155 | Internal: 47155

From: Burrowbridge, Adam <aburrowbridge@wsgr.com>
Sent: Friday, May 8, 2020 6:33 PM
To: Moffett, Dan <dmoffett@AkinGump.com>; Carsten, Douglas <dcarsten@wsgr.com>; Liston, Ian <iliston@wsgr.com>
Cc: WSGR - NanoCellect/Cytonome <nanocellect/cytonome@wsgr.com>; NANOCELLECT (AG TEAM) <NANOCELLECTAGTEAM@akingump.com>; Smith, Rodger (External) <rsmith@mnat.com>; Raucci, Anthony D. <araucci@MNAT.com>
Subject: Re: Cytonome v. NanoCellect | Construction of "Buffer"

EXTERNAL Email

Dan,

NanoCellect does not agree with Cytonome's proposed construction as it does not accurately reflect the relevant claims or specifications. As an alternative construction to the means-plus-function construction NanoCellect initially proposed, to which NanoCellect preserves all rights on appeal, and in accordance with Judge Andrews' order to meet and confer, NanoCellect proposes:

"buffer" means "a reservoir of compressible fluid, configured for absorbing the pressure pulse"

We are available to meet and confer Monday at 1pm ET, should Cytonome wish to discuss the proposed buffer constructions or the forthcoming submission to the Court.

Best,
Adam

From: "Moffett, Dan" <dmoffett@AkinGump.com>
Date: Wednesday, April 29, 2020 at 4:33 PM
To: "Carsten, Douglas" <dcarsten@wsgr.com>, "Burrowbridge, Adam" <aburrowbridge@wsgr.com>, "Liston, Ian" <iliston@wsgr.com>
Cc: WSGR - NanoCellect/Cytonome <nanocellect/cytonome@wsgr.com>, "NANOCELLECT (AG TEAM)" <NANOCELLECTAGTEAM@akingump.com>, "Smith, Rodger (External)" <rsmith@mnat.com>, "Raucci, Anthony D." <araucci@MNAT.com>
Subject: Cytonome v. NanoCellect | Construction of "Buffer"

[External]
Doug, Adam, and Ian,

During yesterday's hearing, Judge Andrews ordered Cytonome to submit a revised construction for "buffer" after first conferring with NanoCellect. Based on our review of the transcript from the hearing and the relevant patent specifications, we propose the following:

"buffer" means "a reservoir of fluid that absorbs a pressure pulse."

Please let us know if NanoCellect agrees with this construction or, if not, identify your specific objections as soon as possible.

Thank you,

Dan

Dan Moffett
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