

We appreciate the opportunity to address concerns regarding textual overlap and image similarities between the following two publications:

1. **Jayant, R.D., McShane, M.J., & Srivastava, R. (2011).** *In vitro and in vivo evaluation of anti-inflammatory agents using nanoengineered alginate carriers: Towards localized implant inflammation suppression. International Journal of Pharmaceutics, 403(1-2), pp. 268-275.*
2. **Srivastava, R., Jayant, R.D., Chaudhary, A., & McShane, M.J. (2011).** “Smart tattoo” glucose biosensors and effect of coencapsulated anti-inflammatory agents. *Journal of Diabetes Science and Technology, 5(1), pp. 76-85.*

The following points clarify **scientific distinctions, image similarities, and editorial concerns** related to these studies.

1. Clarification on Lack of Cross-Citation: Both manuscripts were conceptualized as part of a **larger research investigation on alginate-based drug delivery and biosensor integration**, undertaken by two Ph.D. students working concurrently on closely related aspects of the same system. Due to the interdisciplinary nature of the work, two separate manuscripts were prepared, each addressing a distinct research objective:

- The **Jayant et al. study** primarily focuses on the **anti-inflammatory effects of drug-loaded alginate microspheres** and their role in mitigating foreign body response.
- The **Srivastava et al. study** applies these findings specifically to **biosensor performance, stability, and glucose monitoring in vivo**.

Since both manuscripts were **submitted and under peer review simultaneously**, cross-citation was **not feasible** at the time of submission, as unpublished manuscripts cannot typically be cited in formal scientific publications.

2. Addressing Textual Similarities and Scientific Rationale: We recognize that sections of the introduction, methodology, and conclusions exhibit **overlapping language** due to the shared research foundation. However, key distinctions between the studies exist:

- **Different experimental outcomes:** While both studies investigate the use of anti-inflammatory microspheres, the endpoints differ—one focuses on **implant inflammation control**, while the other evaluates **sensor longevity and glucose biosensor biocompatibility**.
- **Distinct applications of the findings:** The Jayant et al. study provides a **generalized analysis of inflammation suppression**, whereas the Srivastava et al. study applies this concept specifically to **glucose sensor implantation**.

We acknowledge that, retrospectively, greater differentiation in language would have enhanced clarity. However, the **scientific contributions of each study remain distinct**.

3. Addressing Image Similarities and Potential Misinterpretation: Concerns have been raised regarding similarities in pathology and microscopy images across both publications. We provide the following clarifications:

3.1 Justification for Overlapping Images

- Both studies were conducted using **the same experimental setup, and imaging parameters**. As a result, some microscopy images may appear similar however, all images are presented as obtained and fluorescent microscope images with similar loading in them do appear similar.
- The **purpose of these images in each study differs**, with one analyzing **general biocompatibility** and the other focusing on **sensor-specific inflammatory response**.

Justification for Image Similarities

We acknowledge that some images across the two studies appear similar, particularly in the following comparisons:

- **Srivastava Fig. 7A vs. Jayant Fig. 4 (2A, 2B)**
- **Srivastava Fig. 7C vs. Jayant Fig. 4 (2C, 2D)**
- **Srivastava Fig. 6 vs. Jayant Fig. 5 (1D)**

These similarities arise due to the **shared experimental framework** between both studies (control-blank microspheres are same for both). Since both papers focus on **alginate microspheres for implant-based biosensing and inflammation suppression**, histological and fluorescence microscopy images were captured using the **same sample sets**, leading to overlapping visual representations.

Addressing Image Orientation and Time-Point Labeling Concerns

- The observation that **identical images appear under different time points (Day 7 vs. Day 28)**: We acknowledge this discrepancy as an oversight. This was **not an intentional misrepresentation**, but likely a result of an **error in figure assembly or mislabeling** during manuscript preparation.

Addressing Annotation Inconsistencies (Arrows)

- The differences in **arrow placement and annotation** between the two papers reflect **distinct aspects of analysis** rather than an oversight:
 - In the **Jayant et al. paper**, annotations focus on **connective tissue capsule formation** and **inflammatory response** surrounding the implant.
- We understand the importance of maintaining **consistent annotation standards**.
 - In the **Srivastava et al. paper**, the emphasis is on **sensor stability and functional longevity**, which required highlighting different structural changes.

3.2 Addressing Image Orientation and Scaling Concerns

- The microspheres appear nearly identical due to their controlled fabrication process, ensuring uniform morphology and fluorescence properties.

- The observed difference in **scale bar size** between the two articles is due to **image resizing during figure preparation**, rather than any alteration in experimental data.
- If any image inconsistencies occurred during manuscript formatting, they were **unintentional** and do not affect the integrity of the results.

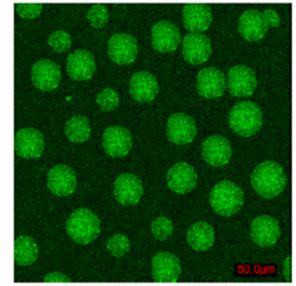


Fig a

See examples of fluorescent images from two different set of experiments (loaded with different dyes for different experiments)

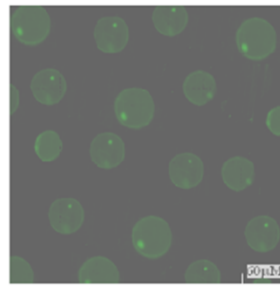


Fig b

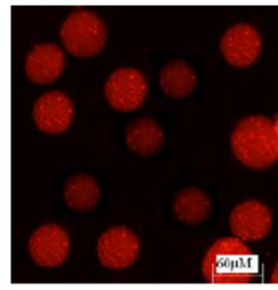


Fig c

The above images highlight different experimental aspects, with color variations reflecting distinct analyses. **Important to note:** any flipping or resizing was an unintentional formatting error rather than deliberate misrepresentation.
