Detection of Trace Aluminum in Model Biological Tissue with Laser-Induced Breakdown Spectroscopy

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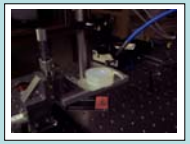


Introduction

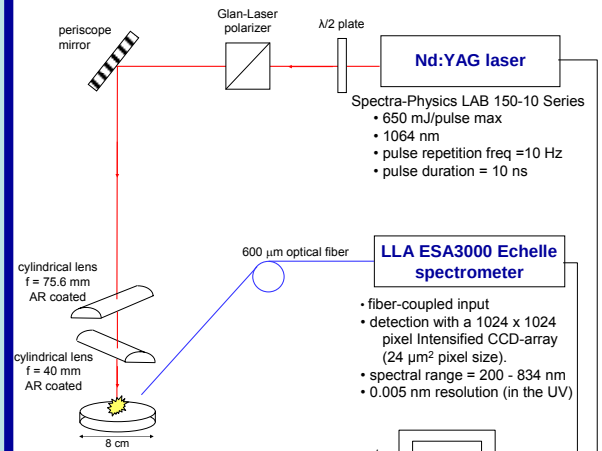
Research at Wayne State University's Smart Sensors and Integrated Microsystems (SSIM) program studies how to restore vision by implanting a micro-fabricated chip into the retina to generate electrical impulses that send a sight pattern to the brain.[i],[ii],[iii],[iv] One concern is that aluminum in these retinal implants is diffusing into the surrounding tissue. Such a deposition of aluminum into retinal tissue could cause adverse performance of the implant and would also deposit harmful metals into the tissue.[v]

In the present work, laser-induced breakdown spectroscopy (LIBS) was studied as a diagnostic technique to assess trace aluminum concentrations in simulated soft biological tissues. The inherent advantages of LIBS such as

- speed
- accuracy
- minimal sample destructiveness
- high spatial resolution on the target surface

all lend themselves to an analysis which could be utilized (potentially *in vivo*) to assess metal concentrations in tissues in which implants have been placed.

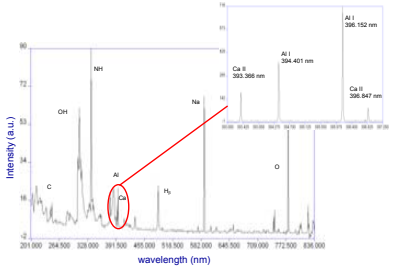
Apparatus



Model Tissue

- 2% electrophoresis grade agarose (Fisher Chemical, BP161-100)
- doped with 20% aluminum-oxide 50 nm nanoparticle / water colloidal dispersion (Alfa Aesar, #12733)
- Al concentrations of 10 ppm to 1000 ppm

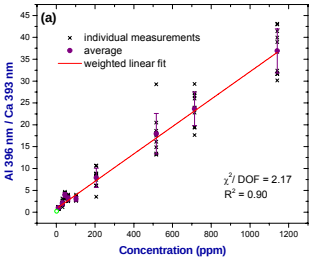
Typical Emission Spectrum



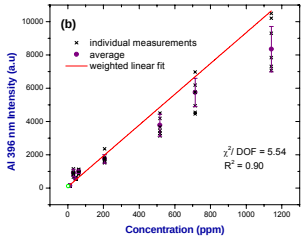
This sample contains
60 ppm Al
Delay after laser delivery
= 6 μs
Gate width
= 20 μs
Laser energy
= 80 mJ/pulse
38 accumulated spectra

Calibration Curves

Standardized samples of known concentrations of aluminum were made and tested to create concentration curves. These displayed a linear concentration-to-line-intensity relationship for concentrations from 10 to 1000 ppm. No saturation of the aluminum lines at high concentrations was observed. Datum from a 2 ppm sample is shown as an open green circle.



Above: Calibration curve using an aluminum line intensity normalized by the intensity of a calcium reference line. This normalization is useful for eliminating noise in measurements of the line intensity.



Left: A non-normalized aluminum intensity calibration curve. A similar relationship between concentration and aluminum line intensity was observed.

[i] T.L. Walraven, R. Iezzi, J.P. McAllister, G. Auner, R. Givens, and G. Abrams, "Biocompatibility of a neurotransmitter based retinal and cortical visual prosthesis," Invest. Ophthalmol. Vis. Sci. **43**, 4453 Suppl. 2 (2002).
[ii] C.A. Jaboro, A.R. Safadi, A.L. Lagman, R. Naik, V. Naik, G.W. Abrams, R. Iezzi, P. McAllister, and G.W. Auner, "A biocompatible study of chronic implants for electrical stimulation and chemical drug delivery to vision," Invest. Ophthalmol. Vis. Sci. **43**, 4476 Suppl. 2 (2002).
[iii] R. Iezzi, N.P. Cottaris, S.D. Elfar, T.L. Walraven, T.M. Raza, R. Moncrieff, J.P. McAllister, G.W. Auner, R.R. Johnson, and G.W. Abrams, "Neurotransmitter-based retinal prosthesis modulation of retinal ganglion cell responses in-vivo," Invest. Ophthalmol. Vis. Sci. **44**, 5083 Suppl. 2 (2003).
[iv] T.M. Raza, R. Iezzi, G.W. Auner, P. Siy, J.P. McAllister, N.P. Cottaris, S.D. Elfar, and G.W. Abrams, "Design of a high-channel-count current source for use in retinal and cortical visual prostheses," Invest. Ophthalmol. Vis. Sci. **44**, 5086 Suppl. 2 (2003).
[v] J.P. McAllister, J. Li, K. Deren, P.G. Finlayson, C. Jaboro, G.W. Auner, R. Baird, A. Lagman, R. Iezzi, and G.W. Abrams, "Chronic in vivo biocompatibility testing of materials used for visual prostheses," Invest. Ophthalmol. Vis. Sci. **45**, 4214 Suppl. 2 (2004).

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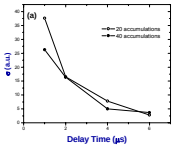
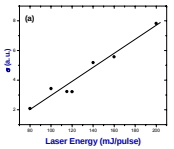
Limit of Detection



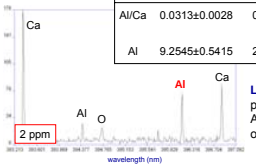


A limit of detection (LOD) was determined from the calibration curves using:

$$LOD = 3\sigma / s$$

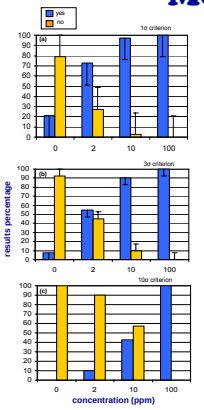
The LOD's were reduced by minimizing the background noise. This was achieved by studying the background noise as a function of delay time and laser energy (**shown left**). Times later than 6 μs and energies smaller than 80 mJ created Al signals too small to be useful.

	calibration curve slope s	background noise σ	LOD (ppm)
Al/Ca	0.0313±0.0028	0.0103±0.0044	0.99±0.43
Al	9.2545±0.5415	2.5438±0.0961	0.82±0.09



Left: This spectrum from a 2 ppm Al sample clearly displays Al peaks and proves that a LOD of 1 ppm is reasonable.

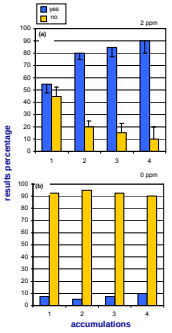
Few Accumulation Measurements

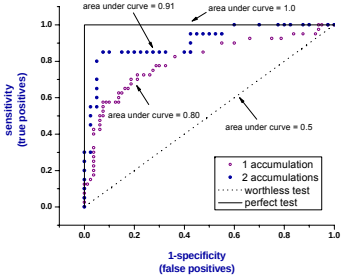


Measurements to create the concentration curves presented above required ~1 in² of sample surface. Therefore, the usefulness of using only a few accumulations requiring only a micron-sized area was also investigated.

Left: Percentage of true positives (yes, Al is seen) to false negatives (no, Al is not seen) for only one accumulation. The 0 ppm sample shows the number of false positives (Al seen when not really there). The three criteria describe the strictness of the test.

Right: A similar test was done using 1 to 4 accumulations which showed that using just 2 accumulations increased the sensitivity by 25% and did not increase the number of false positives.





Left: For clinical applications, the effectiveness of a method is often characterized by a *Receiver Operating Characteristic* (ROC) curve. ROC curves plot the sensitivity of the testing method as a function of specificity. A perfect test (shown as a solid line) remains sensitive at all specificities, especially when there are no false positives. The area under the ROC curve, compared to the areas under the perfect and worthless curves, is a useful figure of merit of the method.