

Optical diagnostics for integrated Advanced Glycation End Products and malignant disease assesment.



P4L09 – Biophotonics, Hven, 2009

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1. Introduction.

Skin auto-fluorescence can be used for diagnostics of malignant tumors. Recently, attention has been drawn to the possibility to measure advanced glycation end (AGE) products by fluorescence. However a number of unrelated natural varying optical properties influence such measurements, thus they need to be assessed and compensated for by multivariate models. We propose an integrated approach for AGE measurements and tumor diagnostics.

2. AGE, biological aging and related risks.

- AGE is accumulated throughout the lifetime of human beings.
- Accumulation rate is increased by oxidative or metabolic stress and environmental factors, e.g. smoking and sun exposure.
- Biological age can be estimated from AGE markers.
- Biological age and spot-wise biological age on suspicious changes are expected to reflect the risk of failure during DNA replication.
- Faulty replication can potentially lead to autoimmune diseases such as malignant diseases, diabetes, Alzheimer and multiple sclerosis.
- AGE measures are suggested for screening and risk estimates for the diseases mentioned.
- Apart from being a biomarker, AGE also acts via AGE receptors, increasing inflammation and decreasing immune response.

3. Perturbations in spectroscopic tumor diagnostics and AGE measurements

- Varying superficial blood distributions absorbs excitation and emission of light.
- Varying natural Melanin concentrations or sun tans absorbs excitation and emission of AGE, weak melanin fluorescence covers the entire visible range.
- Varying body-mass-index (BMI) and related fat layers under the skin might influence excitation and emission light.
- Sweaty skin alters reflectance and transmission for both excitation and emission.
- Lotion, sun screen, perfume, and other chemical contaminants affects reflectance, absorption and fluorescence.
- Varying body hair coverage and melanization of body hair affects by additional fluorescent components.
- Probe pressure inhibits blood circulation and alters optical properties of sampled spot.
- Changing background and atomic gas peaks from fluorescent tubes perturbs spectra.

4. Portable LED based fluorosensor for AGE fluorescence measurements

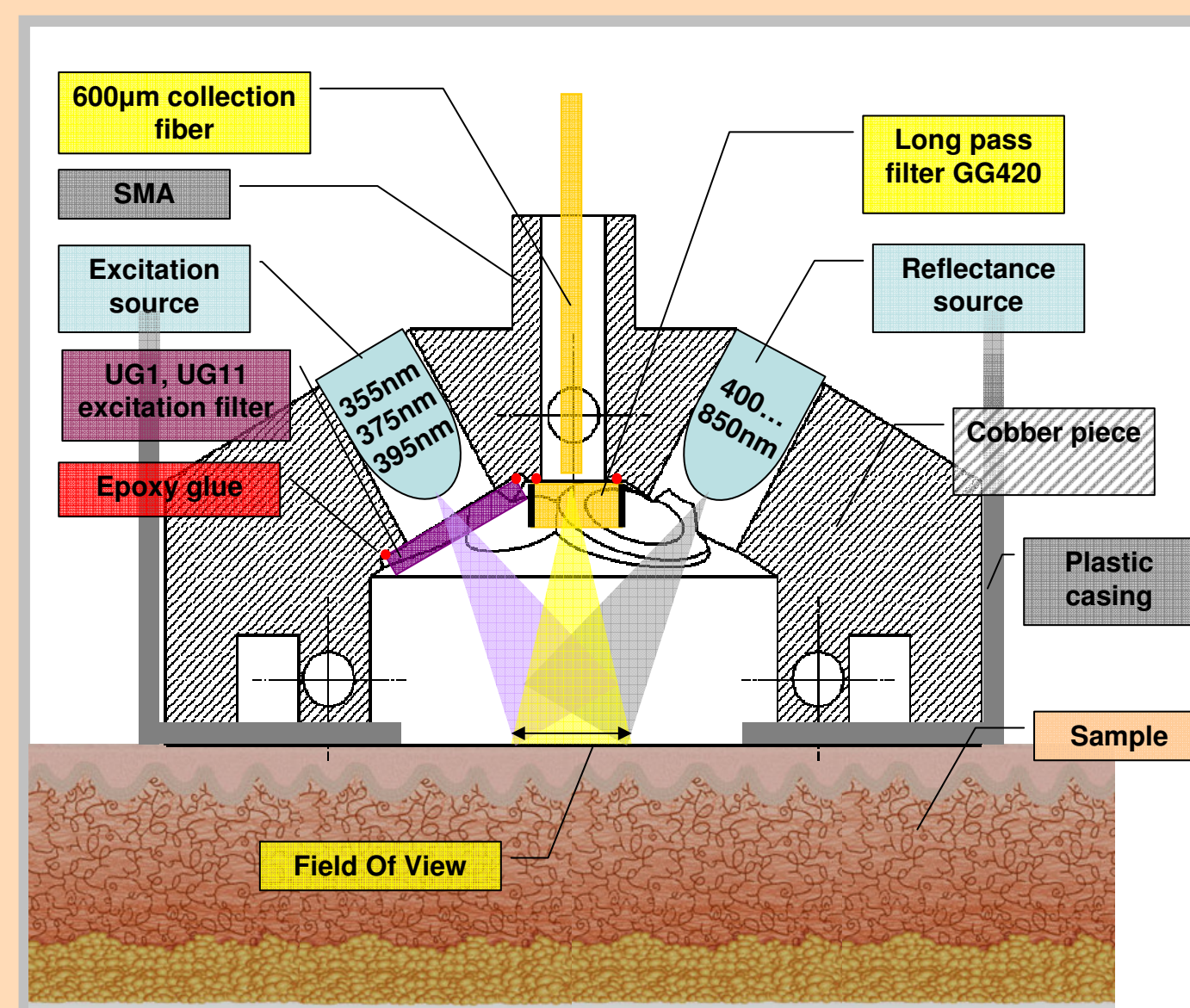


Fig.1: Geometry of mechanical setup for sources, filters and detecting fiber in fluorescence probe. Copper piece is temperature stabilized.

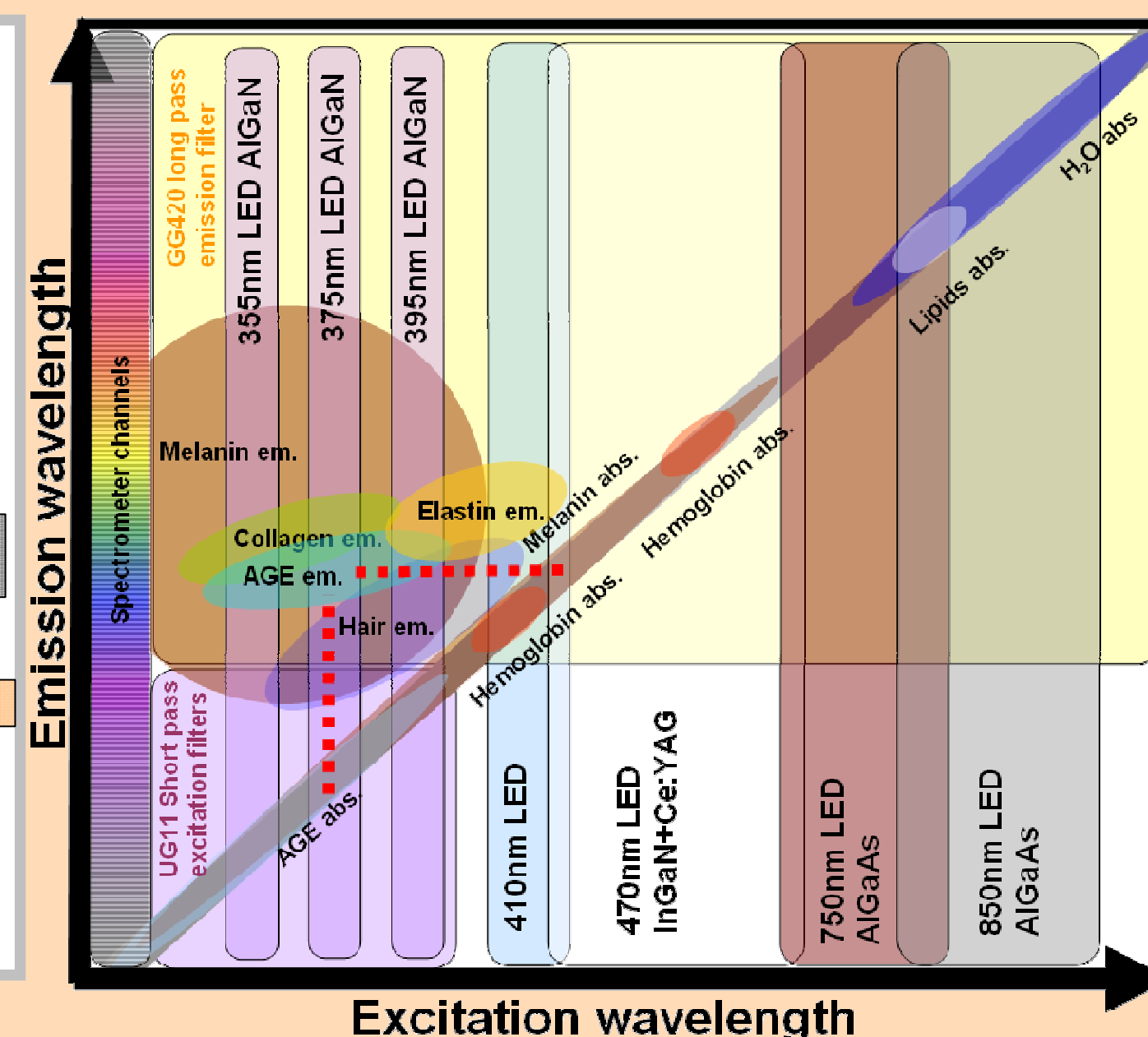


Fig.2: Spectral bands of instrument in respect to dominant spectral components in skin fluorescence measurements.

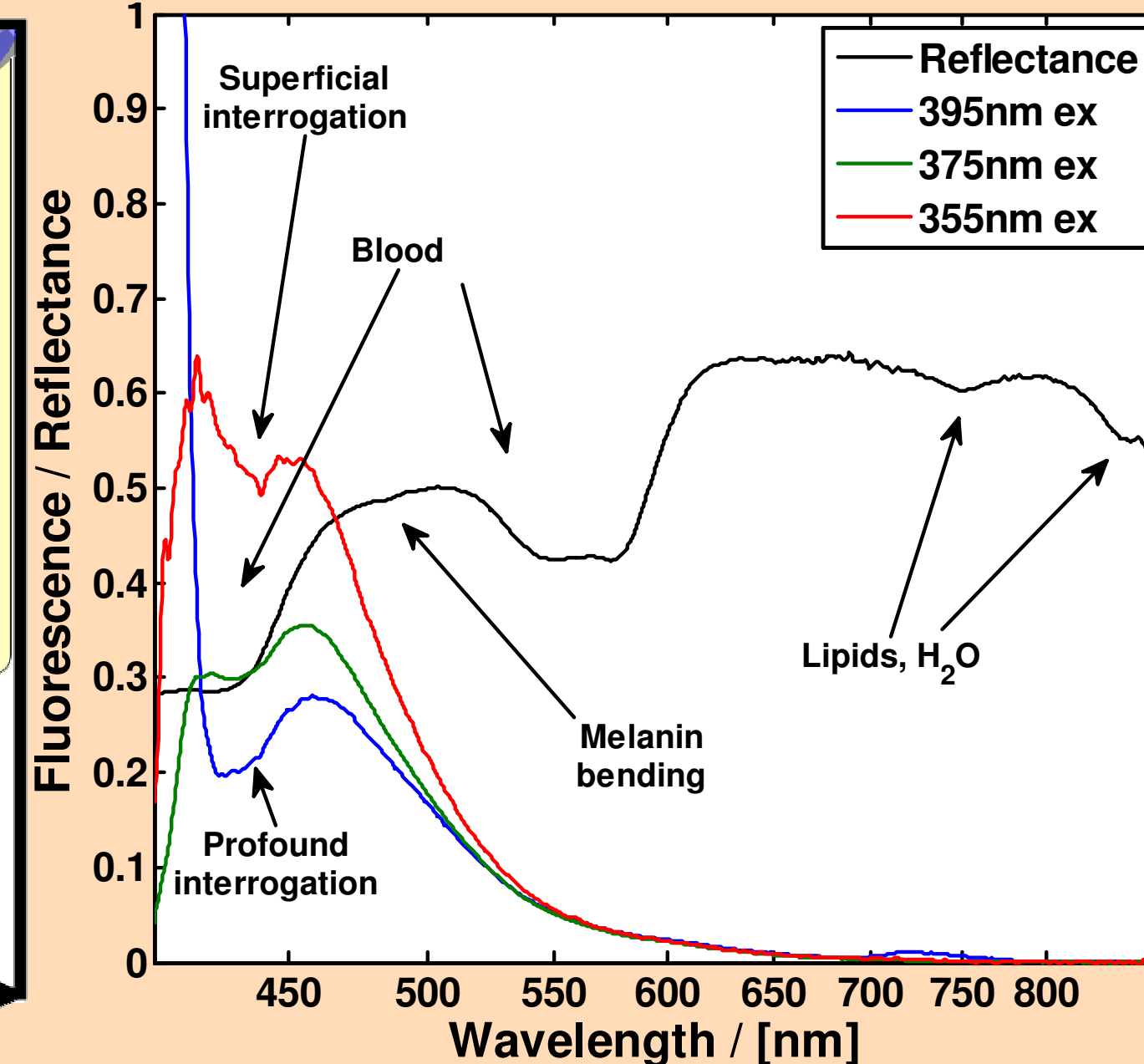


Fig.3: Example of acquired information from one measurement. Three columns and the diagonal are acquired in the EEM.

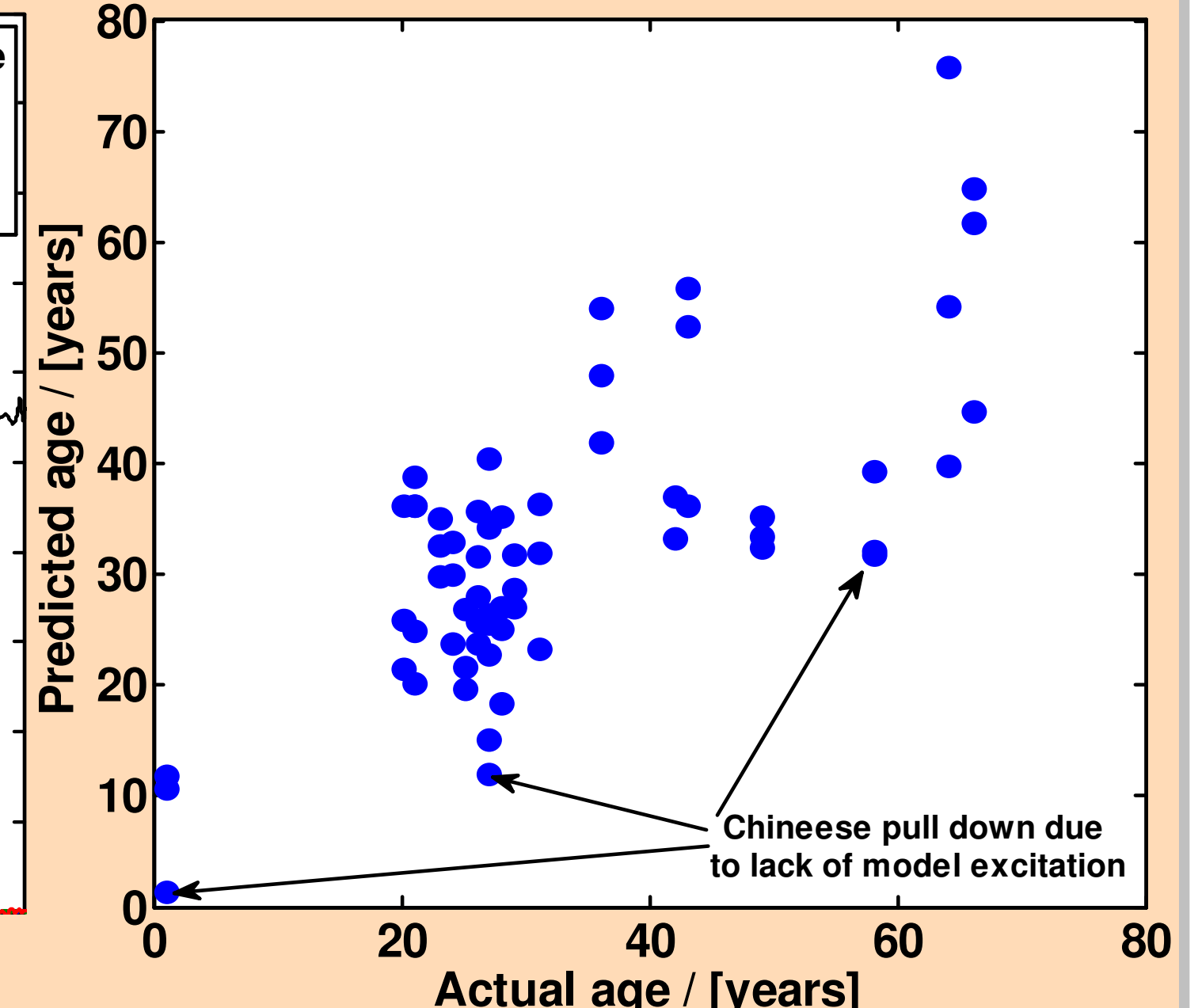


Fig.4: Example of a simple and initial prediction of age based on AGE fluorescence. Sampleset include Caucasians, Africans, Persians, Chinese Asians, and Indian Asians.

5. Design and stabilization.

UI characteristics of each source is assessed to determine band gap which varies with depletion layer temperatures.

Measured band gaps are used for temperature stabilization and prediction of source spectra.

The copper head is regulated by a software PI regulator, heat radiator and a miniature fan.

Excitation sources are equipped with clean-up filters used to suppress emission tails towards longer wavelengths.

The incident angles and non-contact optics is designed to reject specular reflections and varying skin humidity.

Patent is submitted for possible continuation of the development.

6. Results of initial test.

Previous measurements suggest precise age estimation with residual errors of a couple of years. Using training sets requires a broad model excitation, e.g. if the model is based on a young Chinese or young smoker the remaining Chinese or smokers will appear younger. Preferably training sets should include all possible combinations.

Clear correlations in predictions of age and BMI from spectral data have been achieved even in initial tests:

Age: $Rho: 0.72$, $pval: 3.8 \cdot 10^{-11}$

Bmi: $Rho: 0.54$, $pval: 5.9 \cdot 10^{-6}$

7. Future directions

- Improve calibration by including temperature derivatives and CCD temperature.
- Increase sample size, diversity and model excitation.
- Include patients with different malignant skin diseases, and compare spotwise changes to healthy skin.
- Include smokers and diabetics.
- Initial instrument documentation
- Correlate with established AGE measurements.
- Include imager of sample spot, in the sensor head.
- Implementation of Cr:LISAF broad band generation for NIR reflectance.
- Continuation of probe head patent
- Clinical trials.
- Commercialization.
- Development of double dispersive EEM spectrometer.

8. Acknowledgements

This work is supported by a Swedish Research Council project grant and by a Linnaeus Grant to the Lund Laser Centre, Sweden. We thank Benjamin Andersson for help with the initial measurements and Stefan Andersson-Engels, Thomas Svensson and Sara Ek for fruitful discussions. All test persons are acknowledged.

9. References

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