Multi Fluorescence Microsensors for Spatiotemporal Measurement of Culture Environment in a Microfluidic Chip

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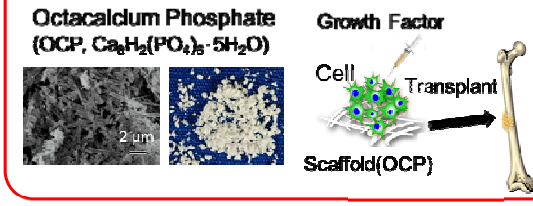
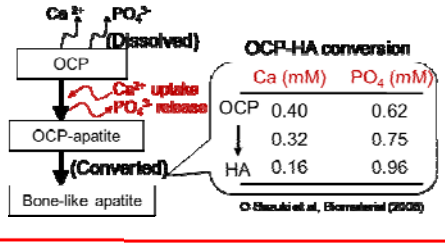
Simultaneous measurement of multi-parameters by single wavelength excitation

Background

Bone biomineralization



Environment measurement during conversion of OCP to hydroxy apatite (HA)

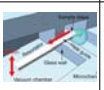
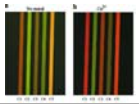


- PO_4^{2-} emitted from OCP during conversion to HA is a trigger of differentiation of osteoblast cell.
- Environment surrounding OCP and differentiation of osteoblast cell have some relationship.

Spatiotemporal measurement of multi-parameters is important.

Conventional approach

On-chip measurement methods

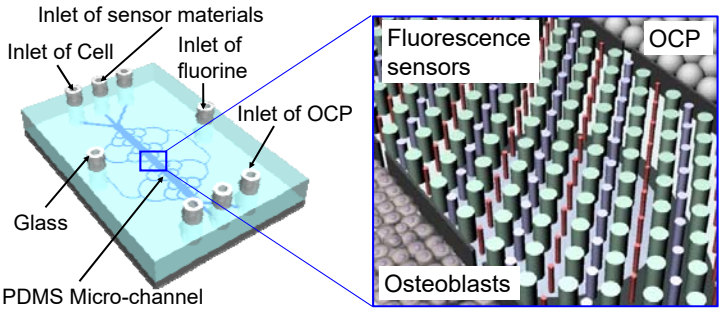
Method	Electric sensor	MEMS sensor	Fluorescence sensor
Schema			
Ref.	Zhiwei Zou, et al, Sens Actuators B,2008	N. Inomata, et al, Appl. Phys. Lett.(2012)	L Basabe-Desmonts, et al, Anal Bioanal Chem, 2008,
Integration of many sensors	Possible	Possible	Possible
Spatial resolution	Low	Low	High

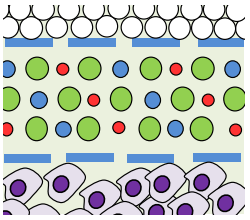
Problems of multi-parameter measurement by conventional fluorescence method

- Limitation of number of parameters
- Low time resolution due to switching the excitation light

Concept

Spatiotemporal measurement using multi fluorescence sensors in a chip





Specification of fluorescence sensors

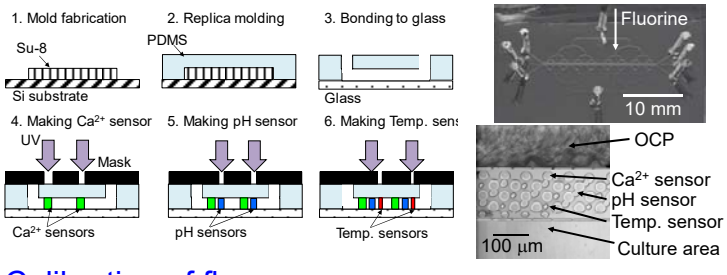
Parameter	Ca^{2+}	pH	Temp.
Sensor material	PEG-DA	PEG-DA	PEG-DA
Fluorescence	Fluo-3	FITC	Lumidot 480
Diameter	20um	15um	10um
Ex.	488 nm	488 nm	488 nm
Em.	527 nm	510nm	515nm

Characters of proposed method

- Simultaneous measurement of multi-parameters by single wavelength light
- No limitation of measurement parameter by arranging sensor shape and pattern

Fabrication of calibration of microfluidic chip

Fabrication process of the chip and sensors

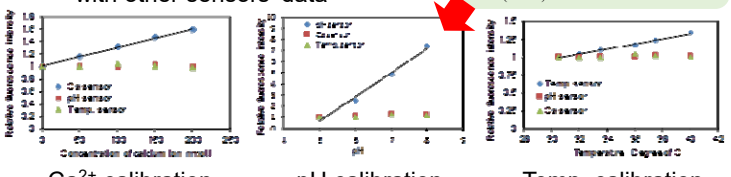


Calibration of fluorescence sensors

FITC is sensitive to both pH and temp.

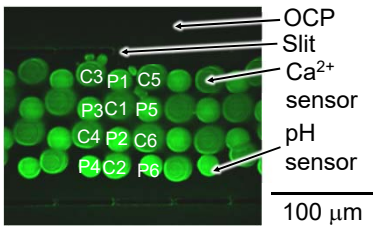
Compensation of calibration with other sensors' data

$$\Delta F_R' = f(pH) \times \Delta T + \Delta F_R$$
$$\Delta F_{R(FITC)} = f(pH) \times \Delta T$$



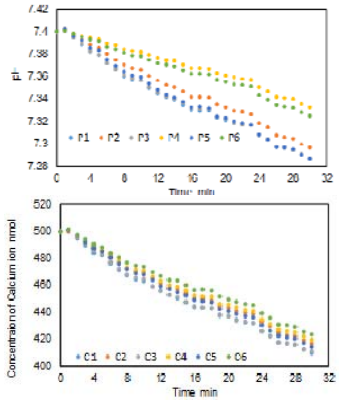
Experiments

Spatiotemporal measurement of variation of $[Ca^{2+}]$ and pH during transformation of OCP to HA



Concentration of fluorine: 100 ppm
Measurement parameter: $[Ca^{2+}]$, pH
Exposure time: 200 ms

Spatiotemporal distribution of $[Ca^{2+}]$ and pH was measured.



Time course variation of $[Ca^{2+}]$ and pH

Conclusions

On-chip spatiotemporal measurement of Ca^{2+} and pH was succeeded using fluorescence multi-sensors.

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Reference: K. Takagi, H. Maruyama, T. Masuda, O. Suzuki, F. Arai, Multi Fluorescence Microsensors for Spatiotemporal Measurement of Culture Environment in a Microfluidic Chip

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