Microelettrovalvola per Bioprinting: prove e misure preliminari

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Bioprinting can be defined as the use of computer-aided transfer processes for patterning and assembling living and non-living materials with a prescribed 2D or 3D organization in order to produce bio-engineered structures serving in regenerative medicine, pharmacokinetic and basic cell biology studies. *(International Conference about Bioprinting and Bio Manufacturing - Bordeaux 2009)*

- **Based on the three “B”:**
  - **Bioink:**
  - **Biopaper:**
  - **Bioprinter:**
Bioprinting workflow

**Process**

1. Pre-processing
   - Cell source
   - Cell culture

2. Processing
   - 3D model
   - Bioink
   - Bioprinter
   - Bioreactor

3. Post-processing
   - Growth factors

**Human Resources**

- **(Bio)Engineer(s)**
  - Design models
  - Run the printer

- **Lab technician**
  - Manage the lab facilities
  - Follow-up printing process

- **Medical Research (MD)**
  - Drive the overall application
  - Evaluates the tissue function

- **Biologist/Biotechnologist**
  - Cell culture
  - Cell function evaluation
  - Biopaper production
  - Tissue growth and assembly
Bioprinters

NovoGen MMX
Not marketed
$180000

3D Bioplotter
$200000

3D Discovery
$200000

BioScaffolder 2.1
Alpha and Omega
BioBots
Inkredible

$12000/18000
$10000
$5000/9000

Refs: https://replicatore.wordpress.com/2015/09/06/top-10-biostampanti-commerciali-2/
BioPrinting project – Lee’s bioplotter

BioPrinting project’s Goal:

Lee’s **Bioplotter**: modular tissue printing platform

1. 4 syringes as “cartridges” to load cell suspensions and hydrogel precursors
2. An array of 4-channel dispensers
3. Target substrate
4. Horizontal stage
5. Vertical stage
6. Range finder
7. Vertical stage heater/cooler
8. Optional independent heating/cooling for the dispenser

*Fig. Lee 2008, Multi-layered culture of human skin fibroblasts and keratinocytes through three-dimensional freeform fabrication*
BioPrinting project – Our approach

- Inspiring by Lee’s bioplotter, this is our purpose:

  Develop a simple work plan, not automated → Integrate the dispenser in a 3D printer → printing proofs (with cells)
BioPrinting project

- **Global setup**: the following material was necessary for the development of the project
  1. Acquisition of pressure signal with 0Psi to 15Psi Gauge Honey-Well sensor, DAQ National Instrument, computer
  2. Acquisition of the piston position signal, to control the valve opening / closing
  3. Air pressurization system
  4. Control Box’s valve
  5. Power supply
  6. Microelectrovalve
Dolphin Fluidics’ DFD-Smart

The DFD-Smart is a modular system with 2-way valves, total isolation, ideal for controlling fluid flows at high hygienic nature and not be contaminated. Each valve can be single, double or coupled in a fluidic block. Each channel can be controlled on-off or proportional independently.

<table>
<thead>
<tr>
<th>Technical Data</th>
<th></th>
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<tbody>
<tr>
<td>Nozzle Diameter</td>
<td>Ø 0.8 mm</td>
</tr>
<tr>
<td>Pressure Range</td>
<td>0 – 4.0 bar</td>
</tr>
<tr>
<td>Operating Temperature</td>
<td>-10° C - +65° C</td>
</tr>
<tr>
<td>Current Range</td>
<td>150 mA – 240 mA</td>
</tr>
<tr>
<td>Response Time @ 0.6 W</td>
<td>180 ms</td>
</tr>
<tr>
<td>Holding Power</td>
<td>0.1 W</td>
</tr>
<tr>
<td>Implementation Power</td>
<td>0.4 – 0.6 W</td>
</tr>
<tr>
<td>Life-time</td>
<td>Million of cycles</td>
</tr>
<tr>
<td>Control</td>
<td>On/Off and Analogic</td>
</tr>
</tbody>
</table>
The purpose of the setup is to measure the performance of the first prototype of the **microelectrovalve DFD-Smart** (Dolphin Fluidics) by drawing a graph of the flow rate $Q$ [ml/min] as a function of working pressure $P$ [mmHg].

Steps of measurement process:

- Pressure signal $P$ [mmHg]
- Valve calibration
- Valve opening time $T$ [s]
- Piston position signal
- Dispensing volume $V$ [ml]
- Plot of Flow rate $Q$ [ml/min]
First setup - Results

- **Testing conditions:**
  - Range pressure from 60 to 150 mmHg
  - Constant voltage of 3.3V (100% of the valve opening)

**Conclusion:**
1. **Low accuracy and precision** of the measurements
2. **Leakage** phenomenon for pressure under 150 mmHg
3. **Channel 2 was clogged**
@ $P = 120$ mmHg: plot of the Flow rate as a function of the valve opening percentage

**Dolphin Fluidics**

**UniPV**

**Channels’ characteristic**

**CH1 flow rate [ml/min]**

**Conclusion:**
1. The measures do not reproduce the *sigmoid curve*
2. Low repeatability
3. Both channels dispensed less than what we expected, because they were clogged
The flow rate was measured by pressurizing a 10 ml syringe, containing H2O

Conclusion:
1. Channel 1 presents more accuracy and repeatability than channel 2
2. Channel 2 dispensed less than channel 1
3. It’s often necessary to clean the channels

CH2 tends to clog easily
Testing conditions for the characteristic of the channels:
- Average working pressure: 120 mmHg
- Valve opening time: 30 s
- Variation of the voltage and of the valve opening percentage

Conclusion:
1. Both channels present a sigmoid curve
2. CH1 dispensed from 0.3V, while CH2 from 0.9V
3. CH1 dispensed more than CH2
Third setup – Results (III)

A step forward: the valve was tested with
- **glycerol solution** to simulate silk hydrogel
- Constant pressure of 120 mmHg
- 100% of the valve opening

**Conclusion:**
1. Flow rate decreases with increasing viscosity
2. Channel 2 dispenses less than channel 1
3. Both channels tend to become clogged, so a frequently clean was necessary
4. The valve is able to dispense up to 25 cP

There is a real possibility of making printing tests with **silk-based solution**
Limitations and future developments

Limitations:
- The accuracy decreases under 100 mmHg of pressure
- Low precision because of the manual control of the dispensing
- Channels tend to clog easily

Improvements:
- Digital control of the pressure signal (constant pressure of 1 - 3 Psi)
- Syringes washing system
- New support for the syringes, to minimize the distance between syringes and the valve
- Automated control of the dispensing

Ackn.: Mr. Pierangelo Bergamaschi
GRAZIE PER L’ATTENZIONE