Single-Port Artificial Pancreas

(or is a single skin perforation enough?)

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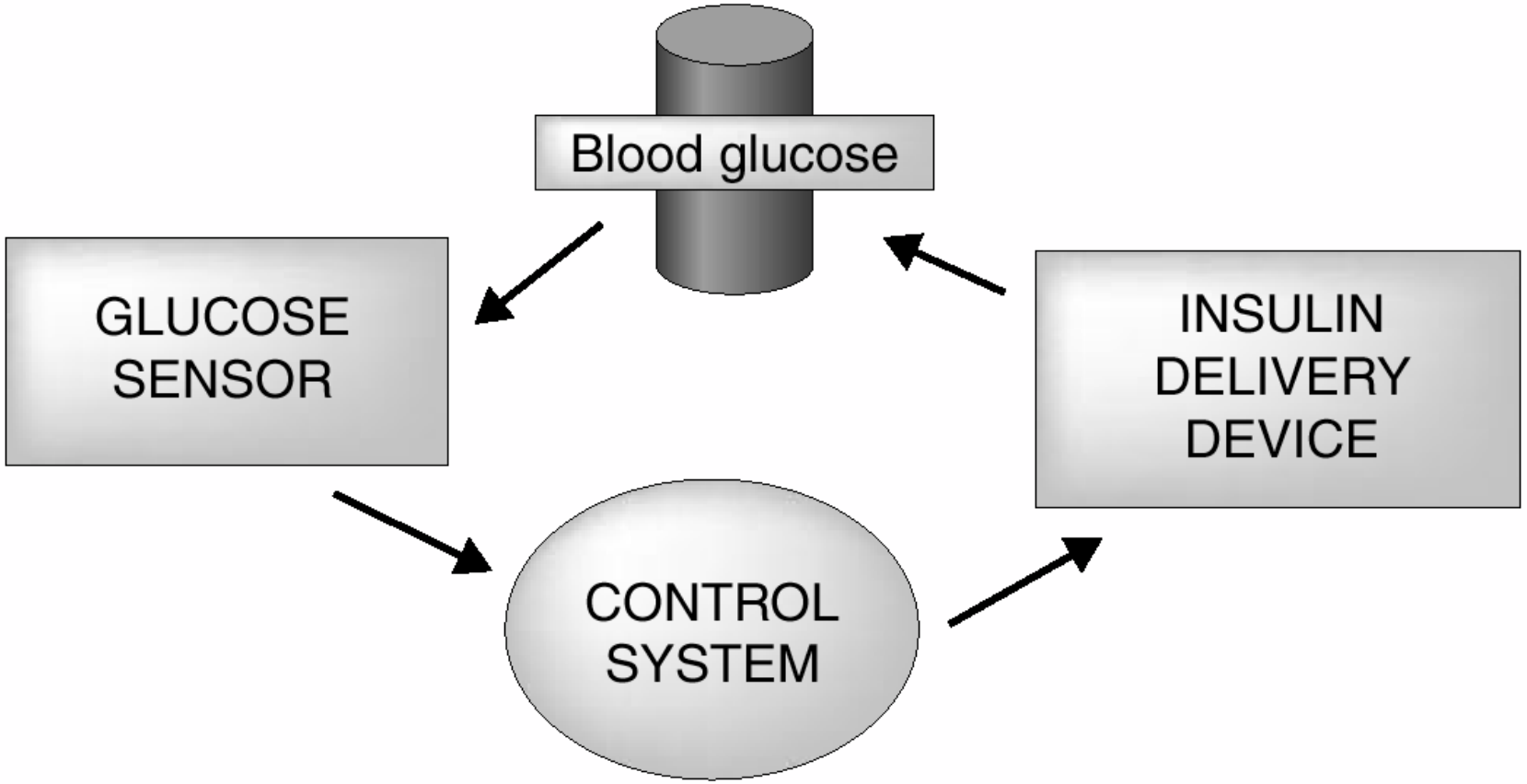
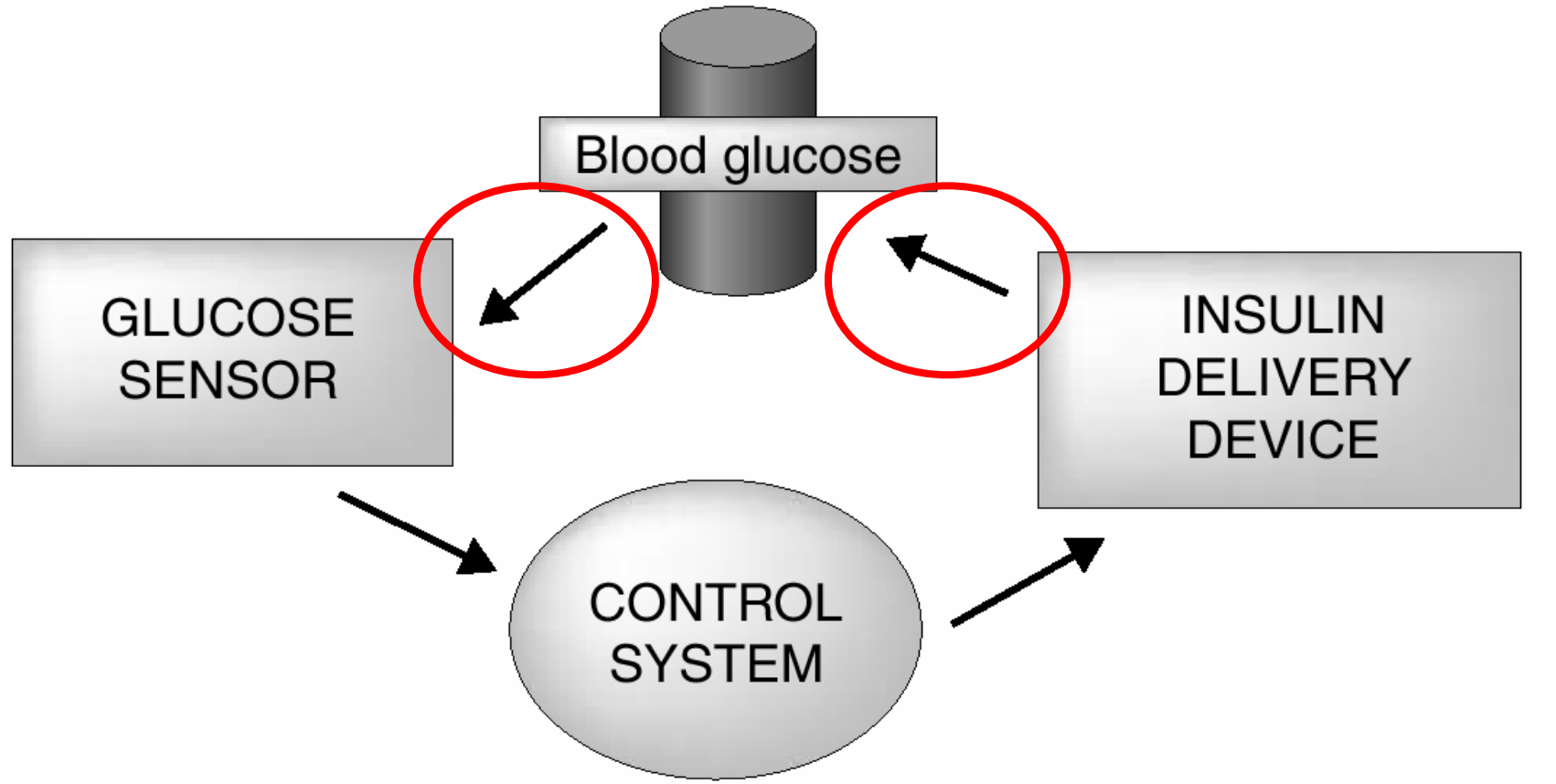
Artificial Pancreas (AP)



Current Opinion in Pharmacology

Little Arrows but Big Issues?



Current Opinion in Pharmacology

Where to Measure Glucose and to Deliver Insulin with AP-Systems?

- **Glucose measurement**
  - **Intravenous (= blood)**
  - **Dermal (= intradermal interstitial fluid)**
  - **Subcutaneous (= interstitial fluid in adipose tissue) (most glucose sensors)**
  - **“Skin” (= mixture of compartments)**
- **Insulin delivery**
  - **Intravenous**
  - **Intraperitoneal**
  - **Subcutaneous**
  - **ARIA: Inhaled, Nasal, Dermal etc.**

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Critical Aspects of Glucose Measurement and Insulin Delivery

- **Glucose measurement**
  - **Intravenous – risky, not long term (?)**
  - **Dermal – time lags, freq. measurements?**
  - **Subcutaneous – limited risks, long term?**
  - **“Skin” – not available yet**
- **Insulin delivery**
  - **Intravenous – risky, not long term**
  - **Intraperitoneal – limited risks, absorption**
  - **Subcutaneous – limited risks, absorption**
  - **Alternative routes of insulin application (ARIA) practicability?**

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Reasons and Issues with the sc-sc Approach

- Most AP-systems employ a two-port approach :
  - Subcutaneous glucose measurement
  - Subcutaneous insulin application
- Reasons:
  - Availability
  - Mature technologies
  - Relatively low risk for the patients
  - Relatively ease of use
- Patients have to carry around two devices all the time: CGM system plus insulin pump
- Patients don’t like this! Major reason for not using CGM systems in clinical trials/reality

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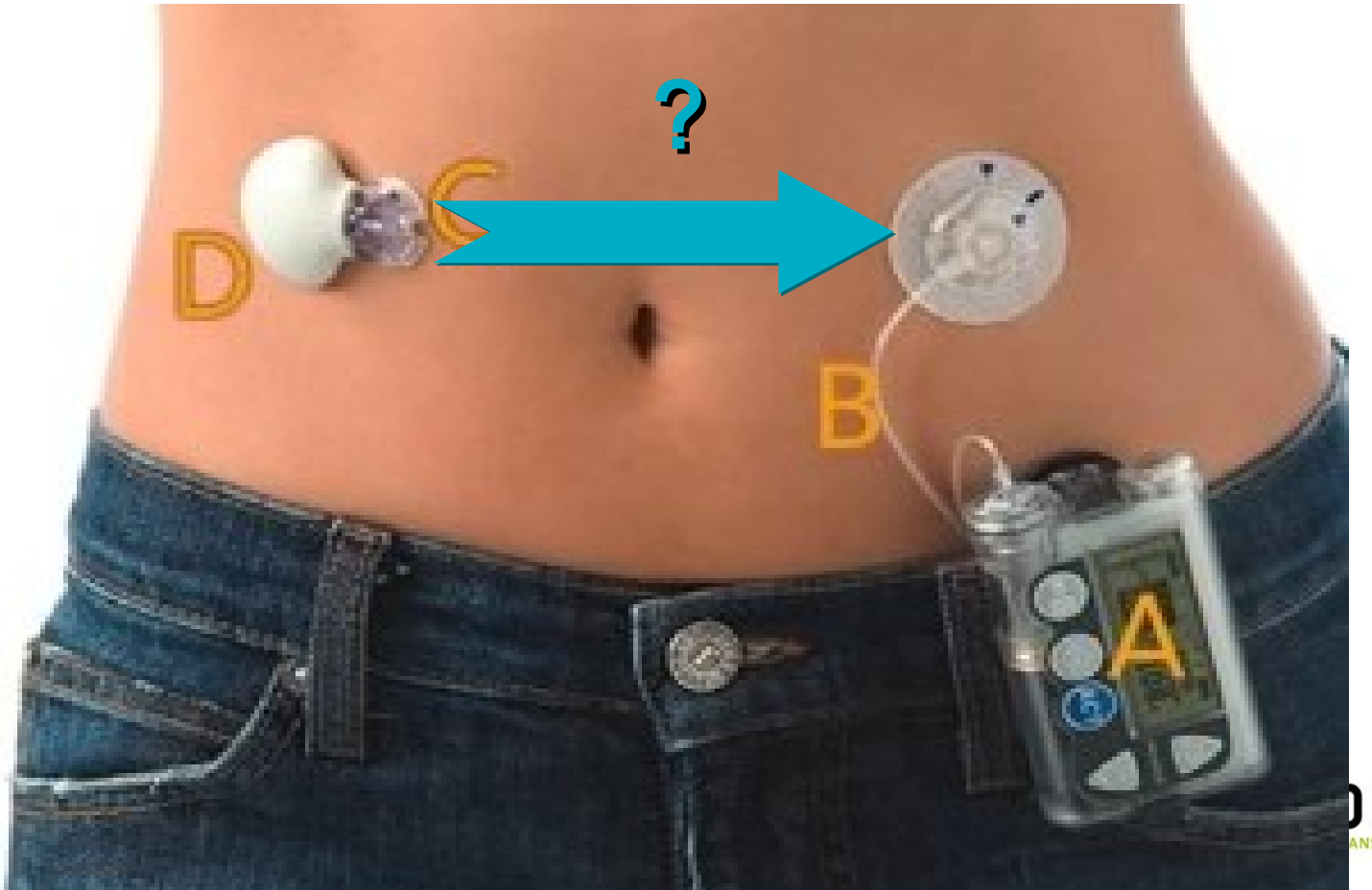
How to Reduce the Hurdle?

- **Single-port approach: Glucose sensing at the site of insulin delivery**



Glucose Sensing at the Site of Insulin Delivery ?

- Key question: Has the insulin infusion an impact on the measured glucose levels?
- Local drop in glucose levels in ISF by infused insulin?
- Deviation of the glucose levels measured in the interstitial fluid from plasma?
- Clinical experiments conducted by the University of Graz showed that a single-port approach is feasible

Lindpointer et al. Diabetes Care 2010a

- **“we found that within 60 min after exposing adipose tissue of healthy humans to a standard 100 units/ml insulin preparation, insulin’s effect on the tissue glucose concentration saturates and a stable ratio between the tissue and plasma glucose concentration is attained.”**

Lindpointner S, Korsatko S, Köhler G, Köhler H, Schaller R, Schaupp L, Ellmerer M, Pieber TR, Regittnig W. Glucose levels at the site of subcutaneous insulin administration and their relationship to plasma levels. Diabetes Care 33:833-838, 2010

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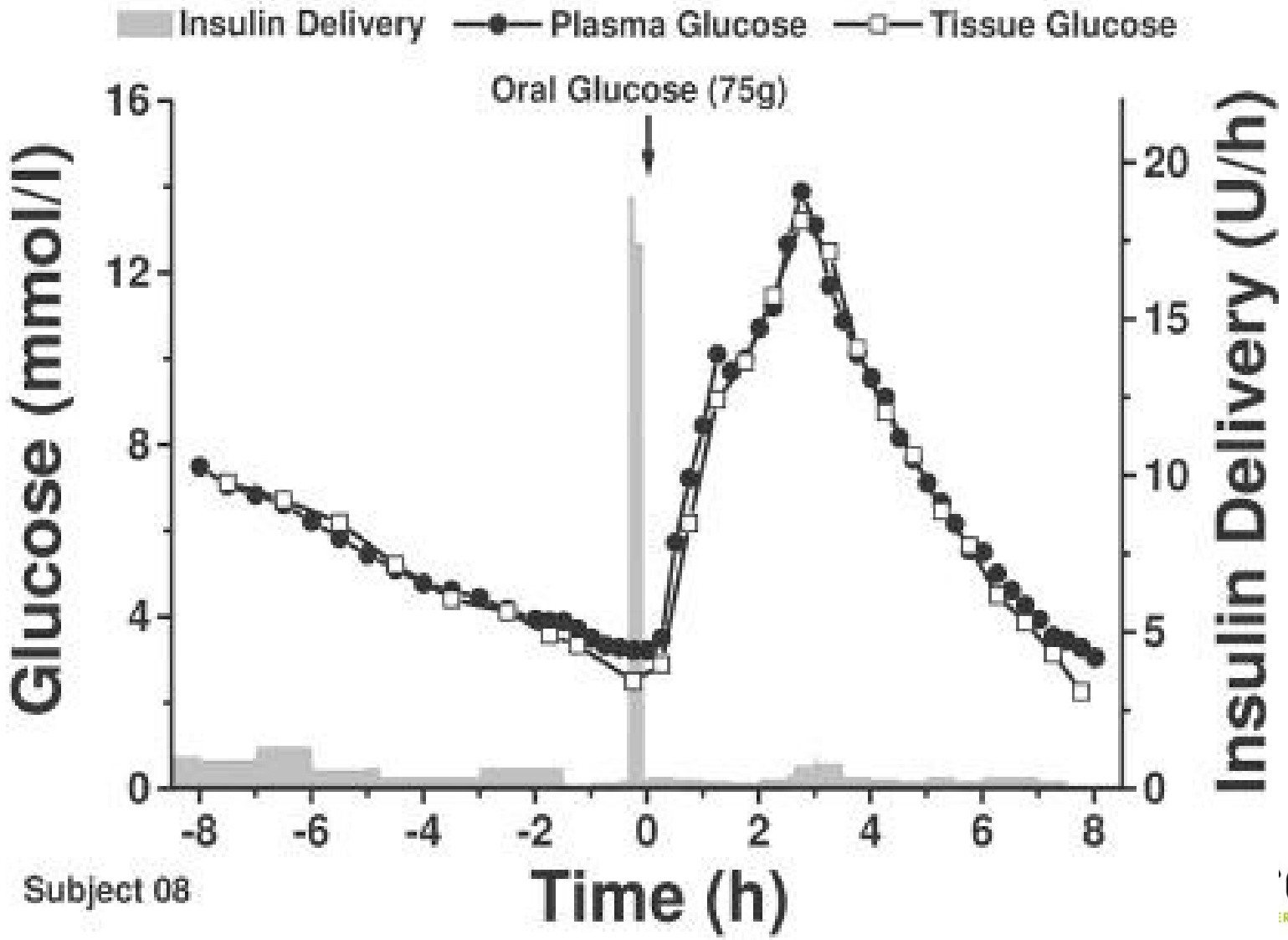
Lindpointer et al. Diabetes Care 2010b

- Insertion of a special indwelling catheter into sc adipose tissue of 10 patients with type 1 diabetes
- Using the catheter for simultaneous insulin delivery and glucose sampling
- Glucose concentration observed at the tissue site of insulin delivery correlates well with that seen in plasma.

Clinical Study with Single-port System



Glucose Sensing at the Site of Insulin Delivery in Practice

- Single-port AP: Is this technically feasible?
- Not experimental set-up but a practically usable product is required
- No international activities to develop the necessary technology, but two different innovative approaches are followed within the EU-project AP@home
- Aim is to have at least one functional single-port AP system at the end of the project

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AP@home

Bringing the artificial pancreas home

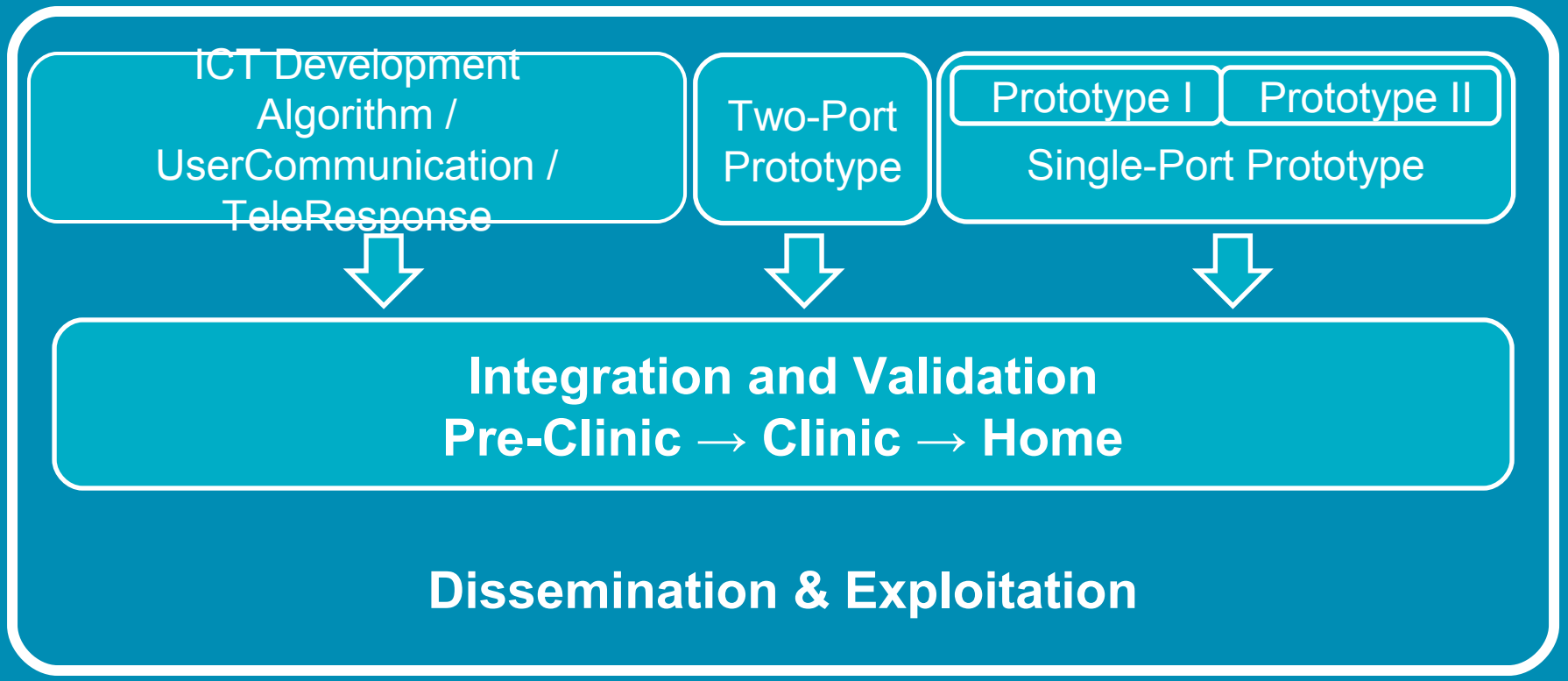
EU Project, funded by 10.5 Million Euro
Started February 1st, 2010
Official Coordinator, L. Heinemann, Profil

AP@home consortium

UNIVERSITY OF CAMBRIDGE

ÉCOLE POLYTECHNIQUE
FÉDÉRALE DE LAUSANNE

Bringing the artificial pancreas home
Major tasks



WP 2.1 Development of New Single-Port Artificial Pancreas Systems

Partners:

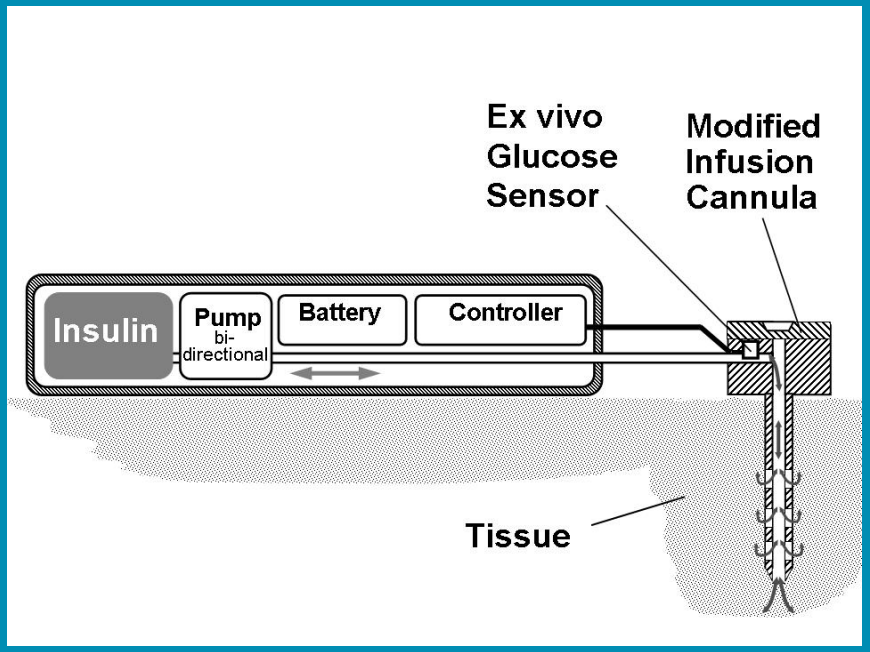
- P4 (GRZ), Medical University of Graz, Austria
- P8 (LAU), EPFL, Switzerland
- P10 (SEN), Sensile Medical AG, Switzerland
- P11 (STM), ST Microelectronics, Italy
- P13 (4A), 4a engineering GmbH, Austria

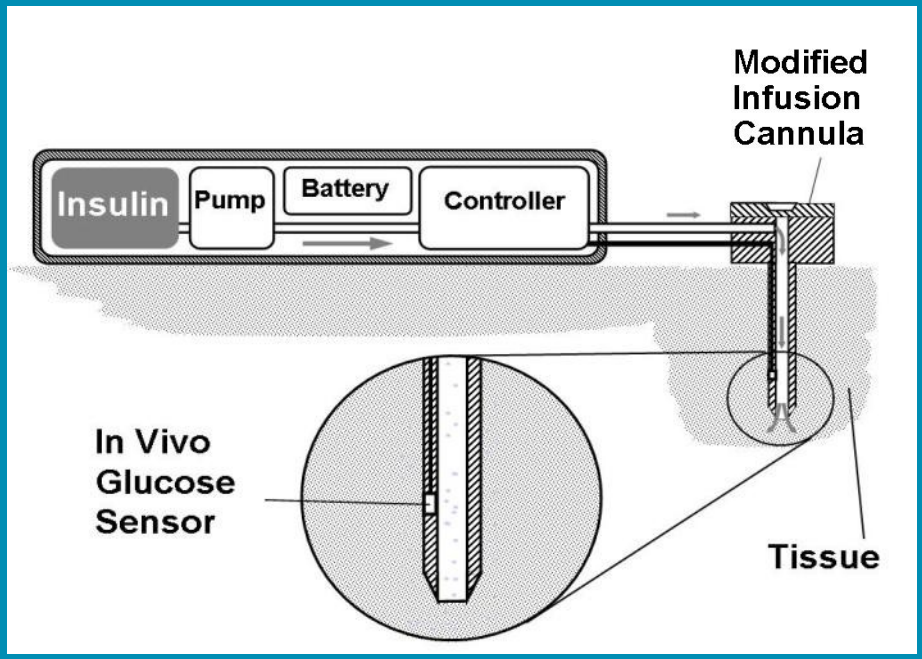
Single-Port Artificial Pancreas Systems
Two complementary approaches

1. **Single-port AP based on insulin cannula with integrated glucose sensor**
   - Combining off-the-shelf glucose sensor with insulin cannula
   - Two sensor placement concepts: *ex-vivo* and *in-vivo*
   - Advantage: proven sensing technology
   - Challenge: assembly of sensor and cannula
1. **Single-port AP based on glucose-responsive membrane**
   - Micro-fluidic approach: measure the flow of insulin through a glucose-responsive porous cannula
   - Adapt established glucose-responsive hydrogel formulations to porous cannula
   - Advantage: tailor responsivity to detection of hypoglycemia
   - Challenge: new measurement principle

TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

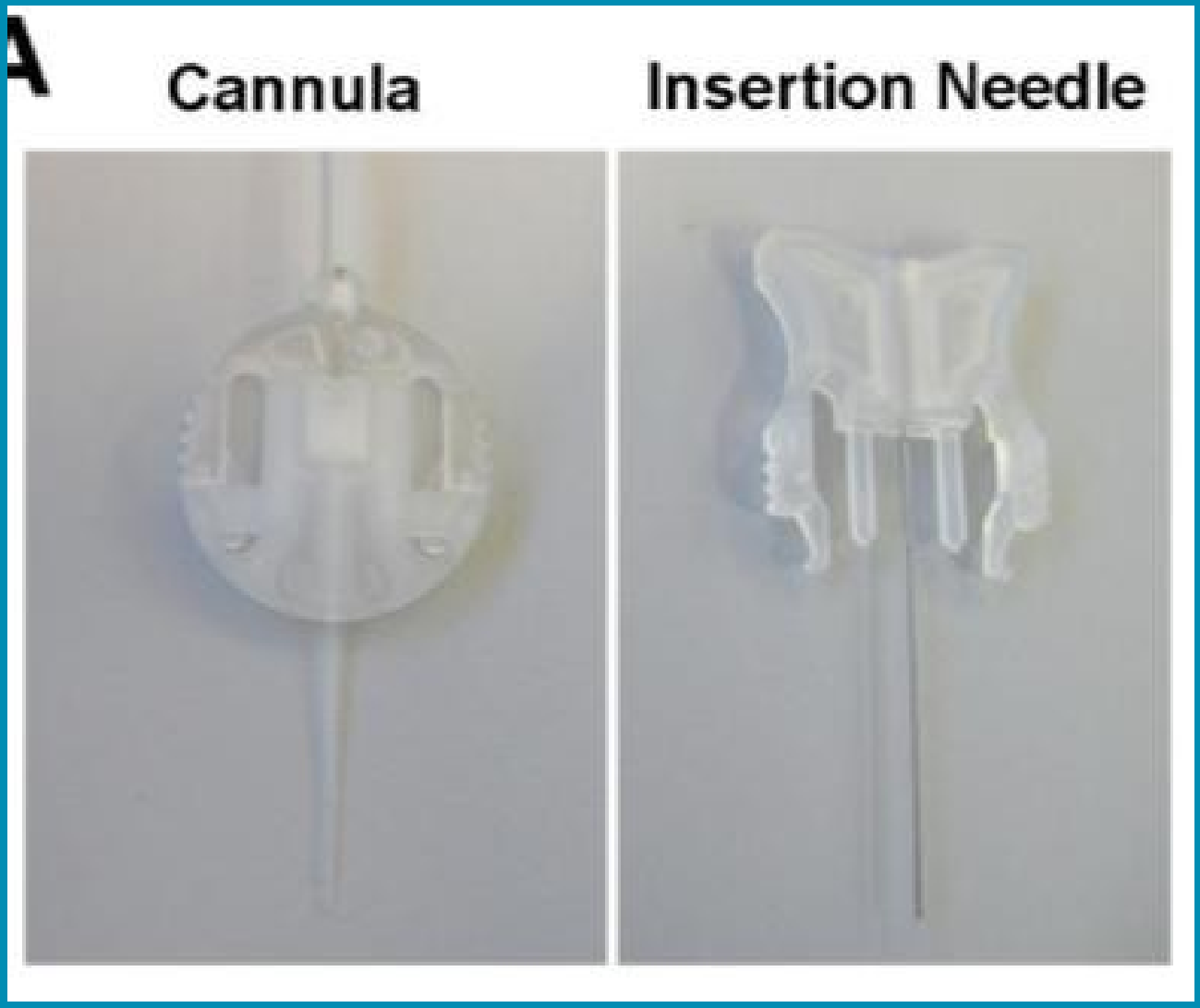
- Two Sensor Placement Concepts
  - ex vivo:
  - in vivo:





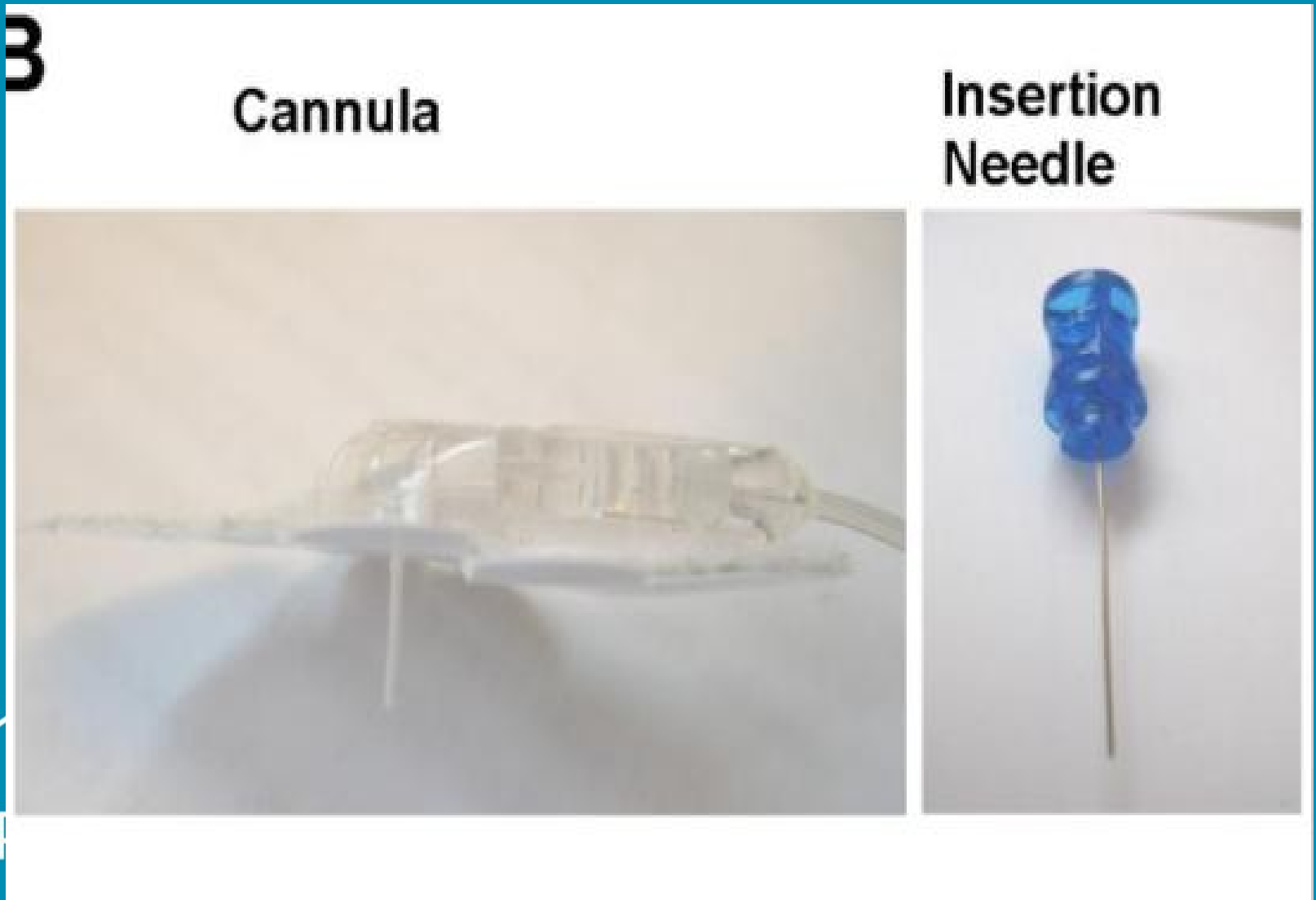
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- - Cannulas with slanted insertion



TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- - Cannulas with straight insertion

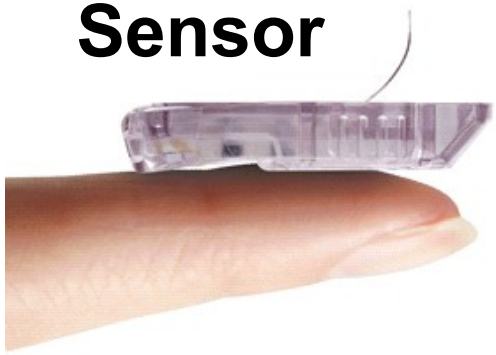


TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

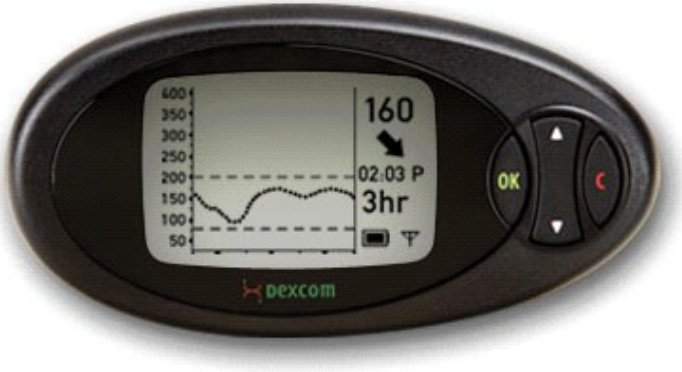
- - Sensors from Dexcom

A

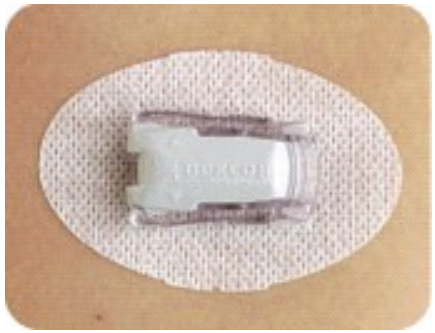
Sensor



Receiver



Inserted Sensor + Transmitter



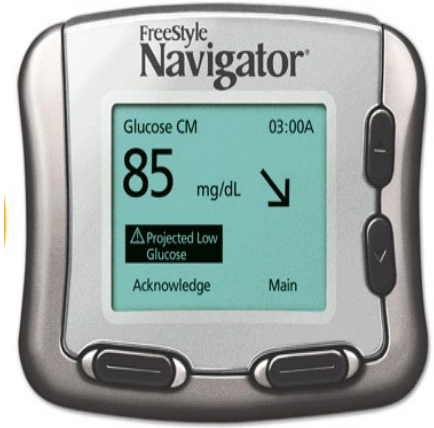
TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- - Sensors from Abbott

Sensor

Support Mount

Receiver



Inserted Sensor + Transmitter

TA 2.1.3: Insulin Cannula with Integrated Glucose Sensor
GRZ/4A Approach

- - Sensors from Medtronic

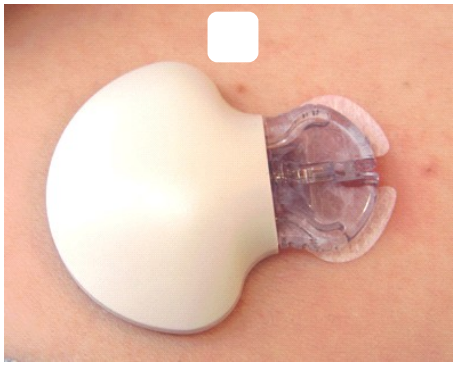
C

Transmitter

Sensor

Receiver

Inserted Sensor + Transmitter



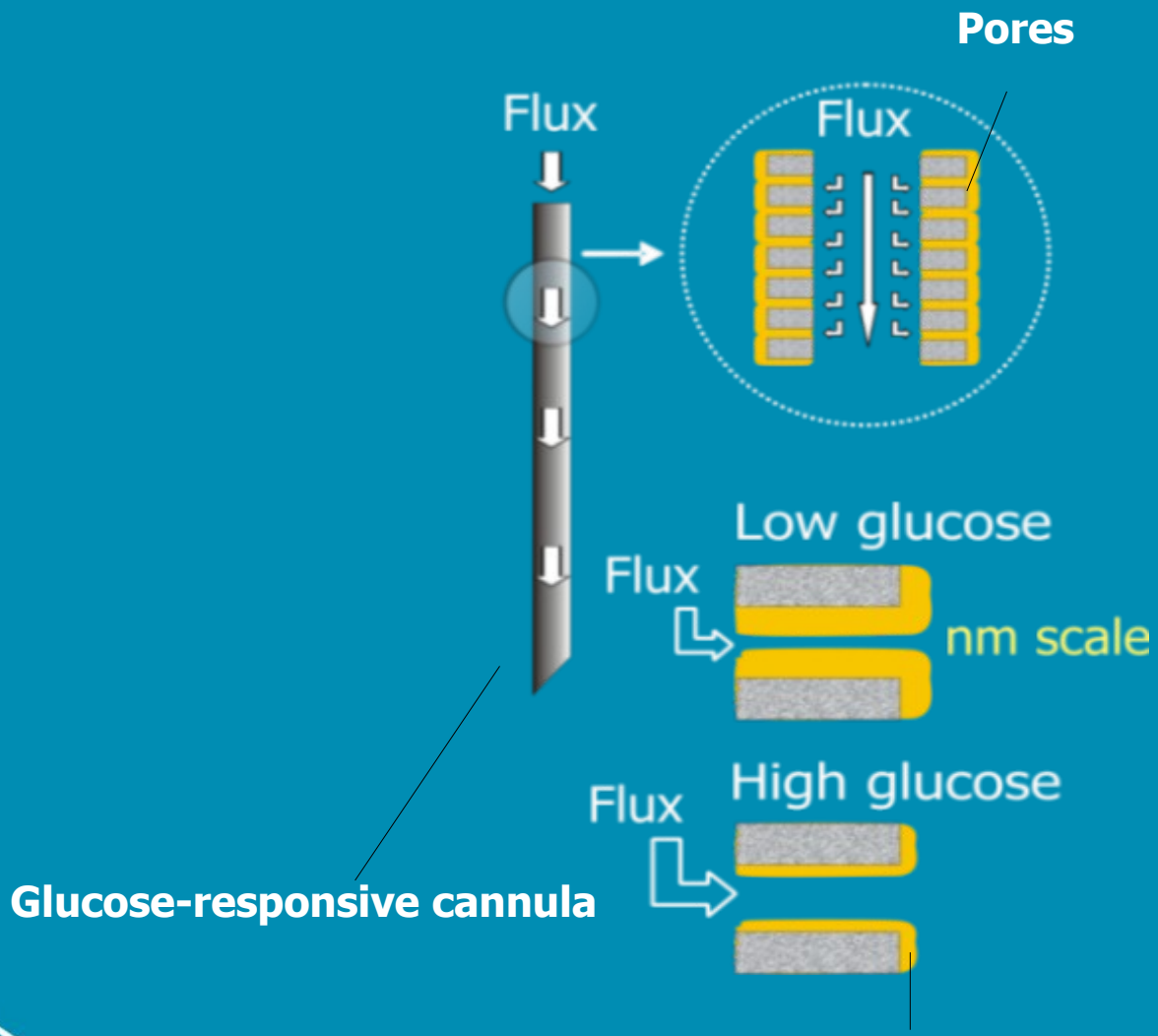
Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach

- **Principle: monitor changes in the flow of insulin administration (pulsed) through a glucose-responsive porous cannula**

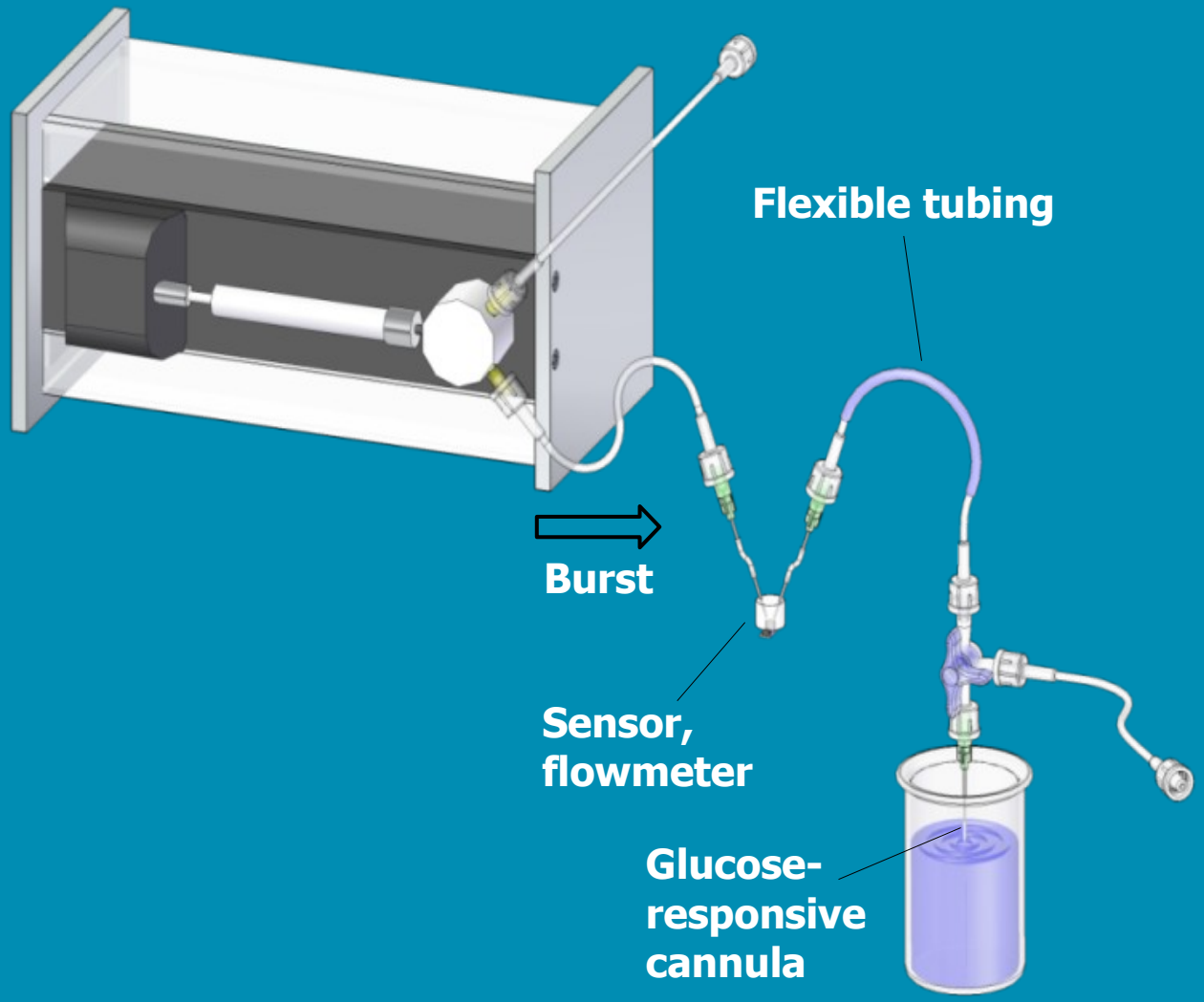
- **Combine insulin administration (basal rate 0.25-1 IU/hr) with measurement of glucose concentration**

- **Core element: An hydrogel trapped in the nanopores of a support membrane swells and shrinks responding to glucose variations.**

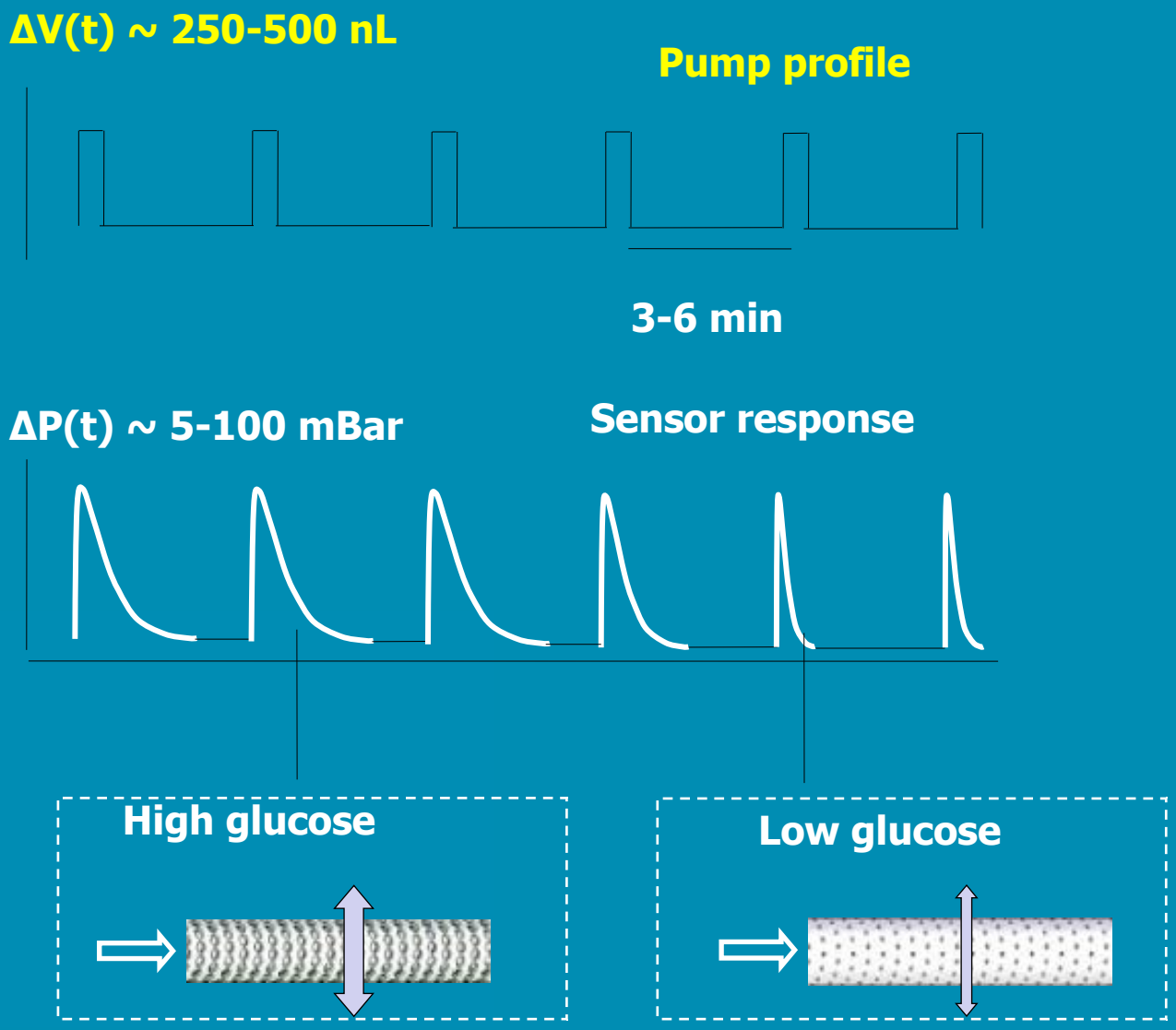
Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach



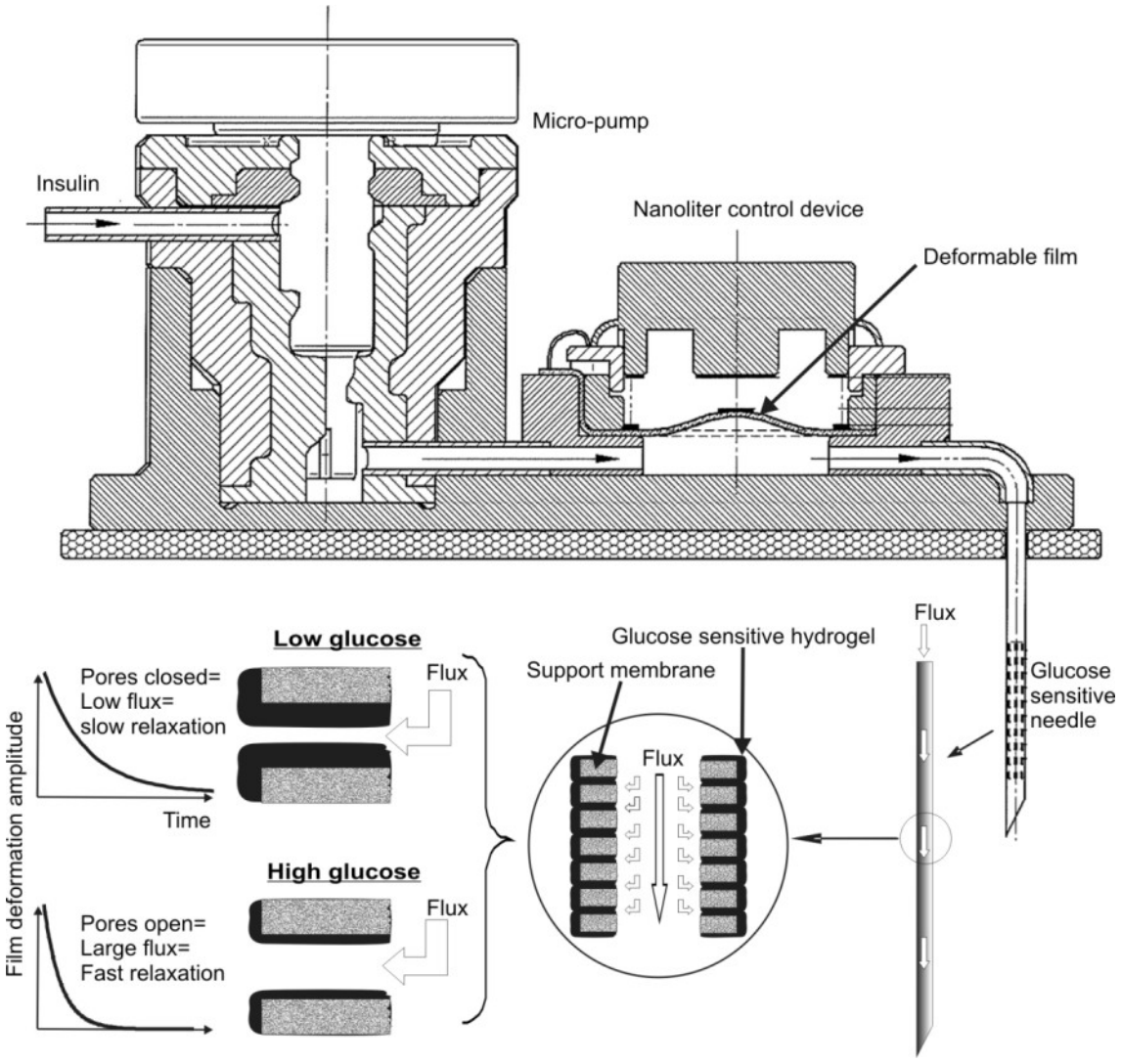
Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach



Single-Port AP Based on Glucose-Responsive Cannula
SEN/LAU Approach

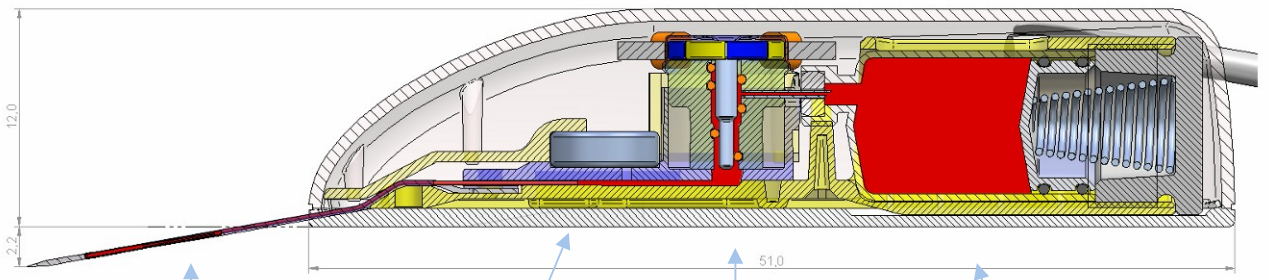


The Sensile Artificial Pancreas
Concept



The Sensile Artificial Pancreas
Possible Embodiment

Artificial Pancreas



Dialysis & Delivery Needle

Micro Pump

Nanoliter Control Device

Insulin

Summary

- Two-port approach for AP systems is the more widely used, patients don't like that many systems are attached to them
- Single-port approach is an attractive and possible alternative!
- Significant reduction barriers towards practical usage of an AP system
- Until now not studied in clinical studies but animal studies are on their way
- Recent developments are very promising
- Clinical data in 1-2 years will proof the validity of my statement

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