

Established: December 1991

Austria Rep. Office  
Steckhovengasse 2/5  
1130 Wien/Austria  
Tel: +43 664 3133223  
[www.unidost.com](http://www.unidost.com)

## MONGOOSE HIGHLIGHTS

- Fulfills a desperate market need
- Improves quality of life
- Eases peace of mind
- Can potentially save lives
- Minimizes or fully eliminates the micro- and macrovascular complications
- Unique & reliable concept
- Fully automated closed-loop glycemic control system

## WORLDWIDE MARKETS

World population	≈ 6.8 G
Diabetes patients	> 220 M
Prediction for 2030	≈ 366 M
Potential MONGOOSE users	> 170 M

## 5-YEAR GOALS\*

- Total MONGOOSE unit sales ≈ 7 M
- Total sale revenues ≈ € 24.42 G
- Total net income ≈ € 555 M<sup>†</sup>
- Further developing our technology
- Capitalize on our success by a business sale, a merger, an IPO, or a management buy-out

\* After starting marketing and mass production

<sup>†</sup> EBITDA

## PROFILE OF THE MONGOOSE PROJECT

### Project Title

Mems-based Continuous Glucose Monitoring with Adaptive Prediction and Targeted Responsive Insulin Delivery

### Preliminary

The MONGOOSE project was initiated, developed, planned and designed by Unidost's founder and president Dr. Mehmet Hendekli, who formed a consortium for the realization of the system. Initially, the funding was sought by the European Commission, and a proposal was submitted to a suitable call in spring 2009. The EC invited the members for a hearing to Brussels – a good indication of technical superb quality for a large scale IP project – and a meeting was realized. Finally, the EC rather considered it to be very risky and its budget to be very high. Needless to indicate that receiving funding from the EC depends on several complex parameters and can be well considered as winning a lottery. Now, we seek other sources and sponsors for the funding of the project.

### Our Mission

To develop and produce market-driven, fully automated closed-loop glycemic control system, utilizing our consortium's extensive engineering and medical expertise.

To start with the worldwide introduction and marketing of the MONGOOSE system, a wearable minimally invasive miniaturized device that functions as a kind of artificial pancreas for the diabetes mellitus patients.

### MONGOOSE Device

The device will be achieved through MEMS technology, will be attached to the skin of the patient, will continuously monitor the interstitial glucose level, automatically deliver insulin when necessary with respect to the glucose level measurements, automatically and adaptively predict the patient-specific diabetes behaviour after processing sufficient samples of measurements and actions, and wirelessly transmit the results to a remote unit and/or control center for screening and information purposes.

### Unmet Need

Prolonged hyperglycemia causes serious macrovascular (ischaemic heart disease, stroke and peripheral vascular disease) and microvascular (retinopathy, nephropathy and neuropathy) complications and death, whereas also prolonged hypoglycemia states lead to sudden coma stages and again death. Checking blood glucose level and delivering insulin several times a day is mostly painful and inconvenient for the patients that are usually limited in their daily activities. Patients, families, caregivers, internists and endocrinologists are in desperate need for a simple, reliable, minimally invasive, inexpensive system that can provide 24/7 closed-loop diabetes control in order to prevent complications and tragedies, enhance the quality of life of the patients, and improve their medical conditions.

## MONGOOSE CONSORTIUM

Dr. Mehmet Hendekli (UNIDOST)  
MONGOOSE developer and  
consortium manager  
T: +43 664 3133223  
E: hendekli AT ieee DOT org

Dr. Thomas Velten (Fraunhofer  
Institute)

Prof. Stefan Dimov (Cardiff  
University)

Dr. Etienne Hirt (Art of  
Technology AG)

Prof. Claes-Göran Östenson  
(Karolinska Institute)

Prof. Cees Tack (Radboud  
University Nijmegen Medical  
Centre)

Prof. Sudhesh Kumar (University  
of Warwick)

### Status of the MONGOOSE

We are already in a mature stage of this project in terms of having addressed several challenging issues and having found a satisfactory resolution for many problems (in several manner like microfluidics, modeling, patient-specific insulin delivery algorithm, etc.). On the other hand, we also completed a deep competitor analysis and carefully structured our pricing scheme.

### Business Model

We will position the MONGOOSE as the sole, wearable monitoring and closed-loop glycemic control device for diabetes mellitus, and maintain a leading position should ever a direct competitor enter this niche market. We will set up an internet infrastructure to enable direct purchases by patients, parents and caregivers, and establish worldwide distribution and technical service hubs. We will price the MONGOOSE device so that the product will be financially attractive for direct consumer sales and distribution via pharmacies and agents.

### Financial Needs

In order to conclude the design, implementation, prototyping, clinical trials and validations, approvals from regulatory bodies, starting mass production and commercialization, and subsequently commence marketing the MONGOOSE device, Unidost as the consortium leader is seeking immediate funding on behalf of the consortium. We are in need of approx. € 10 M over a period of 48 months. Detailed milestones, workpackages, deliverables, our marketing plan, budget profiles, etc. are available.

## MONGOOSE PROJECT – EXECUTIVE SUMMARY

Without doubt, the disease diabetes mellitus, which describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both, is a great burden for the whole planet affecting millions of people worldwide. Recent WHO (World Health Organization) calculations indicate that worldwide almost 3.2 million deaths per year are attributable to diabetes mellitus with an alarming increase in the trend. It is projected that the total number of diabetes patients in the world will increase to 366 million by the year 2030. It is a chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. There are three forms of diabetes mellitus in the broad sense:

**Type 1 diabetes mellitus:** This is actually an autoimmune disorder that results in the permanent destruction of insulin producing beta cells of the pancreas. This form of diabetes mellitus is insulin-dependent meaning that these patients need insulin treatment to survive.

**Type 2 diabetes mellitus:** This is caused by the body's ineffective use of insulin, which often results from excess body weight and physical inactivity. It is characterized by disorders of insulin action and insulin secretion, either of which may be the predominant feature. Some of these patients may also require insulin treatment for control, however in some rare instances even for survival.

**Gestational diabetes mellitus:** This is carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy, which generally resolves once the baby is born. However, women with gestational diabetes are at increased risk of developing type 2 diabetes mellitus after pregnancy, while babies born to mothers with gestational diabetes are at increased risk of complications.

Among the above three forms, type 1 diabetes mellitus and especially the insulin requiring version of type 2 diabetes mellitus pose a great risk of macrovascular (ischaemic heart disease, stroke and peripheral vascular disease) and microvascular (retinopathy, nephropathy and neuropathy) complications. Although there are currently some new therapy approaches under development, the common method is measuring the blood glucose level and delivering insulin when necessary usually by injection or insulin pump. Checking blood glucose level and delivering insulin several times a day is mostly painful and inconvenient for the patients that are usually limited in their daily activities, and furthermore it is based on manual check, although there are some automated glucose sensors, either already developed and approved by the appropriate bodies, or currently under development and tests, which at least try to automate one component of the whole treatment approach. Even some artificial pancreas approaches are currently under development, but no success has been achieved so far. And for the current continuous glucose monitoring systems, none of them are based on MEMS (Micro-Electro-Mechanical Systems) technology and provide the highest convenience and efficiency.

Hence, our project is based on the fact and motivation that diabetes mellitus is a great burden for the patients and world's economy, that a very efficient and fully automated therapy system is needed, which will provide full freedom and convenience to the patients in their daily activities, and minimize or fully eliminate the associated complications of this disease, and that such a similar unique, inexpensive, disposable and accurate system is currently not existing.

Our project is a mainly application focussing complete engineering and scientific work that also involves some degree of research and development of new technologies for the unique design of the proposed product, small series production of prototypes, and clinical trials on diabetes patients. Our target audience consists of the following components:

- Type 1 diabetes mellitus patients and insulin-treated type 2 diabetes mellitus patients (end-users).
- Clinical trial centers (clinical studies).
- Health authorities (regulatory issues).
- Hospitals, clinics, medical centers (prospects).
- Engineering, scientific and medical community (researchers) who may be interested in our results, know-how and technology.
- Industrial actors who may be interested in incorporating our technology into their systems (integrators).
- Investors who may be interested in investing in a venture for marketing.

Our main objectives can be summarized as follows:

- To design a proper functioning prototype of the intended device.
- To successfully pass clinical trials and approvals.

- To fully eliminate or significantly minimize the associated severe complications of diabetes mellitus at the patients.
- To provide the patients with utmost efficiency, accuracy, comfort and convenience in therapeutical aspects and daily life.
- To eliminate or minimize the financial burden of the disease.
- To improve the quality of life and the general life expectancy of the patients.
- To provide a precise tailor-made patient-specific behaviour profile based on complex adaptive prediction algorithms.
- To open up doors for further visions and research in this area.

The main benefits of our project obviously lie in significantly contributing to the fight against diabetes mellitus through a fully automated continuous painless glucose monitoring and responsive insulin delivery system, and thus in improving the quality of life and the general life expectancy of the patients with type 1 diabetes mellitus and insulin-treated form of type 2 diabetes mellitus. The aimed device will be an inexpensive, disposable system in micro dimensions, which will replace the daily burden of such patients in applying the same therapy approach conventionally through several manual checks and painful deliveries. The total therapy costs of such patients will be reduced, and furthermore enormous financial savings in the health system are expected through reduced number of cases developing any severe complications of the disease. Additionally, other invaluable benefits will be creating a patient-specific disease behaviour profile that will be used for future predictions, and preventing the reactive depression that most of such patients experience after they have been diagnosed with this chronic disease. Hence, both the physical and associated psychiatric complications are prevented.

We are precisely addressing the following target outcomes:

- Firstly, our focus is on automated closed-loop glycemic control in the daily life of the patient, i.e. at home and outside.
- We intend to design a minimally invasive painless system that will both perform continuous monitoring of the glucose level with acceptable measurement error levels (i.e.  $\leq 5\%$ ) and providing hypo- and hyperglycemia alarms, where the latter case will also automatically activate insulin delivery.
- The system will adjust itself to the specific diabetes profile of the specific patient through complex adaptive prediction algorithms.
- Results and actions will be transmitted to a remote unit and/or control center through wireless communications.
- Components will be integrated into a miniaturised device incorporating micro features.
- Utmost accurate and reliable measurements are targeted.
- Automated control of the disease will be provided, as well as opportunity to process and analyze data from a remote control center.
- Education and feedback to patients and physicians will be provided.

It has to be noted that the advantages of using MEMS technology as the core part of our design concept can be summarized as follows:

- As all current available glucose sensors are not long-term stable, i.e. have a short life-span, they need to be exchanged quite frequently resulting in a lot of discomfort and pain for the patient, if they are invasive sensors. However, MEMS technology will enable us to design microneedles and biosensors of suitable length, such that our

system would act in a minimally invasive manner causing no pain or discomfort at all for the patient, as the nerve endings or pain sensors beneath the skin would not be touched in our system.

- Hence, in our approach a minimally invasive MEMS unit, whose frequent replacement (e.g. every 48-72 hours) would not cause the problems associated with other approaches, will be used. Of course, additionally, our approach will allow continuous glucose monitoring instead of measurements at some points of time (i.e. lancing the fingertip). It has to be emphasized further that our system would allow the continuous glucose monitoring in the real sense meaning to achieve it for lifelong duration just with easy and comfortable replacements of a disposable part of the MEMS unit to be designed, whereas all other existing approaches would require painful procedures instead.
- A further feature of our system is that the insulin pump will also be a MEMS design, i.e. also minimally invasive. Hence, the whole concept will be realized and implemented in one minimally invasive MEMS system forming the core of our proposal or approach.
- Compared to all other existing approaches, through fully automated continuous glucose level monitoring, responsive insulin delivery and adaptive prediction, our system will provide the optimum conditions to achieve the maximum duration of desired target glucose levels in a day, thus eliminating, reducing or delaying the micro- and macrovascular complications of the diabetes disease.

At this point, the main benefits and advantages of our proposed system and approach can be concluded as follows:

- **We do address both type 1 diabetes mellitus patients and insulin-treated version of type 2 patients unlike all past and current advise-you open-loop systems and closed-loop algorithms in research settings only that were developed for diabetes mellitus type 1 patients only.**
- **We will perform both continuous glucose monitoring and automatic responsive insulin delivery, i.e. a fully automated closed-loop glycemic control.**
- **Our innovative closed-loop algorithm is better than existing algorithms, because for the first time in literature in this work we will introduce new concepts into the conventional insulin regimen initialization and adjustment schemes. Our algorithm, which will much more closely mimic the natural person specific plasma profile of the endogenously secreted insulin, will be based on these new concepts.**
- **We use a very innovative design and MEMS technology which in our case provides the following important advantages: Cheap disposable comprising glucose sensor unit and insulin delivery unit, minimally invasive and thus painless, and no problems with long-term stability of the sensor because it will be replaced frequently (only possible because cheap and because not associated with pain).**
- **Depression related patient behaviour of neglecting the therapy will be avoided.**
- **We introduce polymer-based innovative processes for cheap mass fabrication of microneedle arrays.**
- **We provide remote disease management and hypo-/hyperglycemia alarms management.**

The patient will receive all vital details on the screen of the device that he/she will wear on the skin as a wristwatch. Hyperglycemia states will already be addressed automatically in our

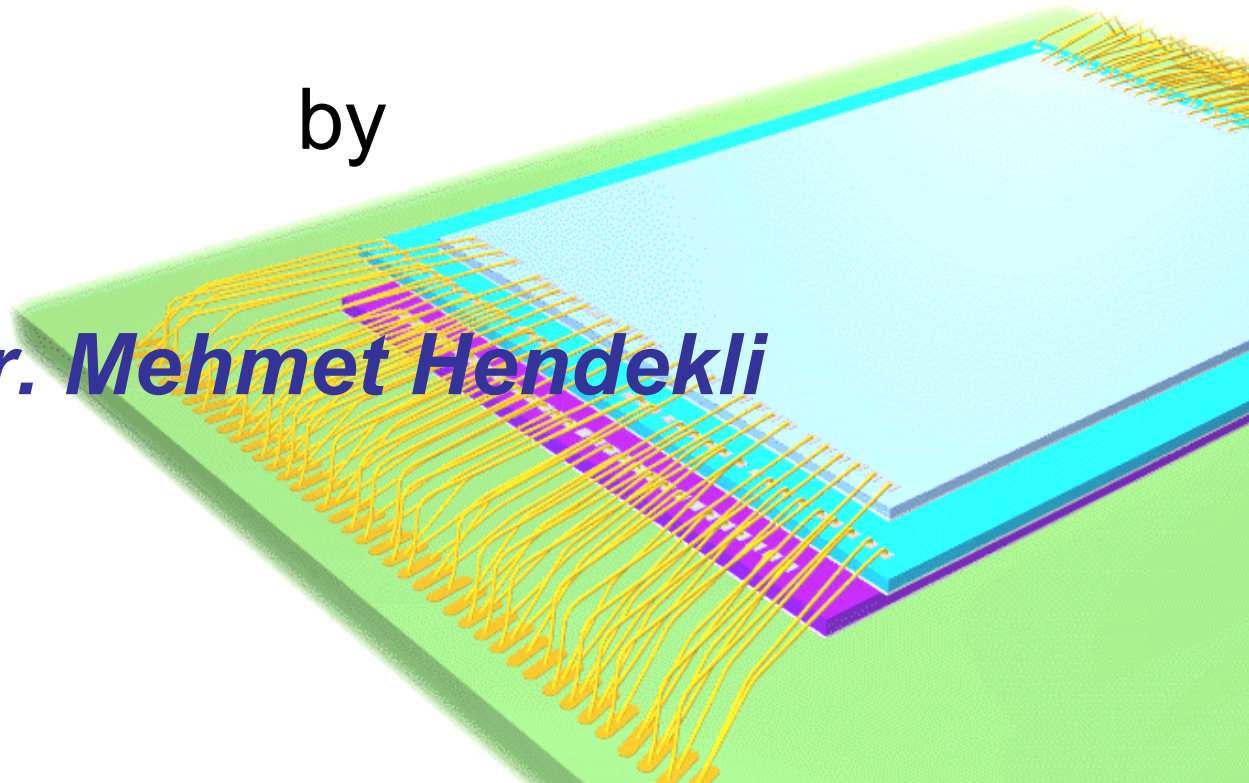
system such that the insulin delivery will be initiated by the pump. Hypoglycemia states in a very early starting phase **without reaching dangerous and harmful limits**, will appear as an alarm on the screen guiding the patient to dextrose ingestion or carbohydrate intake.

Moreover, the remote control center will enable physicians and observers either manually and/or automatically through software implementation with detection algorithms to perform an efficient crisis management. The parameters will also be displayed there continuously, and the physicians can either manually inform the patient, or execute actions through communicating with the device from the interface and implemented software, or even program the software such that these actions can be performed automatically. However, those are just features of our proposed approach that are just thought to be implemented as **additional protective mechanisms**. Our device is already an automated closed-loop system that will handle the alarming states on its own, except the possible hypoglycemia states in the current plan. However, even any possibility of hypoglycemia states is extremely low, as our system will not allow this through its automated monitoring and responsive reaction mechanism, as we will perform continuous glucose monitoring in the real sense meaning that sampling will be done within intervals of a few seconds unlike all previous related monitoring systems.

# MONGOOSE PROJECT

by

*Dr. Mehmet Hendekli*



# **Mems-based Continuous Glucose Monitoring with Adaptive Prediction and Targeted Responsive Insulin Delivery**

## **MONGOOSE**

## CLOSED-LOOP GLYCEMIC CONTROL

**No system is currently working as a closed-loop outside of short-term research settings!**

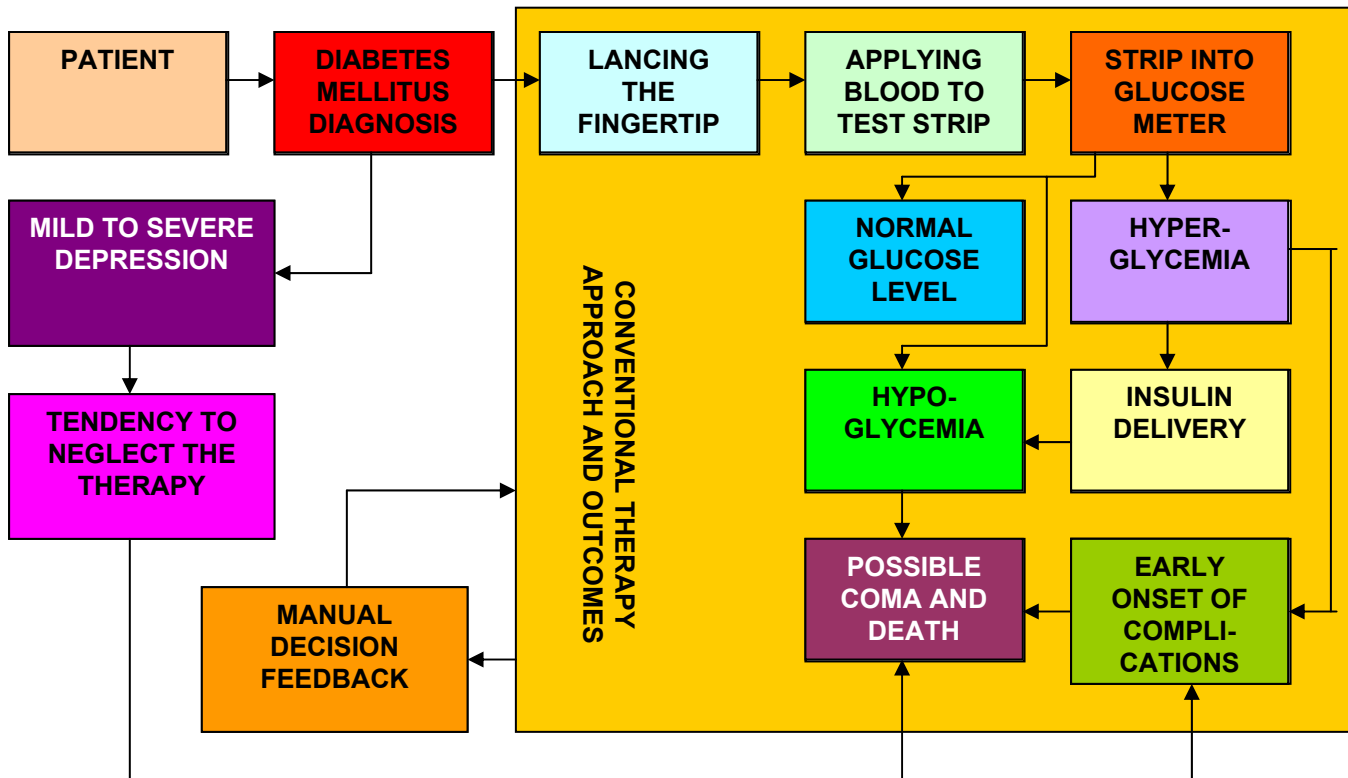
For humans, the control algorithms were **externally employed as decision support systems** or in simulation studies using individualized patient models.

The current success of such systems and algorithms is **very limited** and they are **not applicable to humans in practical terms for long-term duration** due to several concerns including safety and reliability. Experts predict a time interval of  $\geq 10$  years for the first launch of such devices on the market.

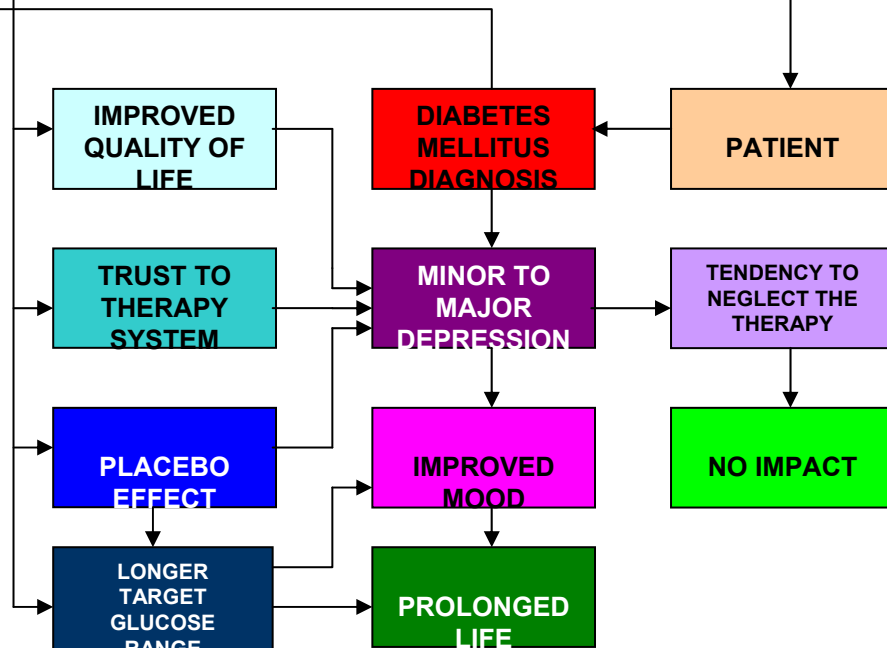
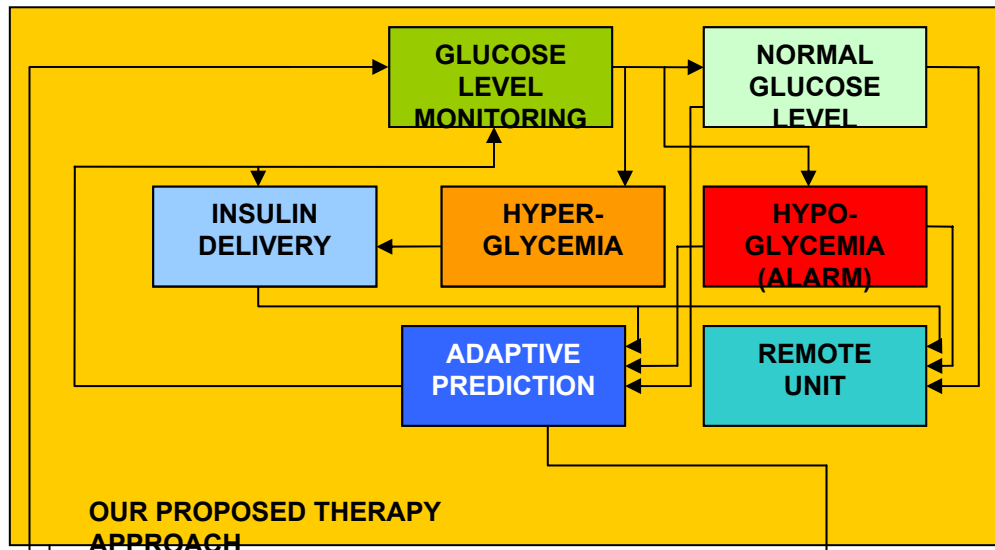
No system is currently designed in an inexpensive and comfortable manner that can be worn by the patient continuously without any limitations.

All past and current closed-loop algorithms were developed for **diabetes mellitus type 1 patients only** without taking into account the insulin-treated version of type 2 patients, **whose physiopathology is quite different**. However, in **MONGOOSE** we do plan an approach **that will equally address the needs of both type 1 and type 2 patients!!**

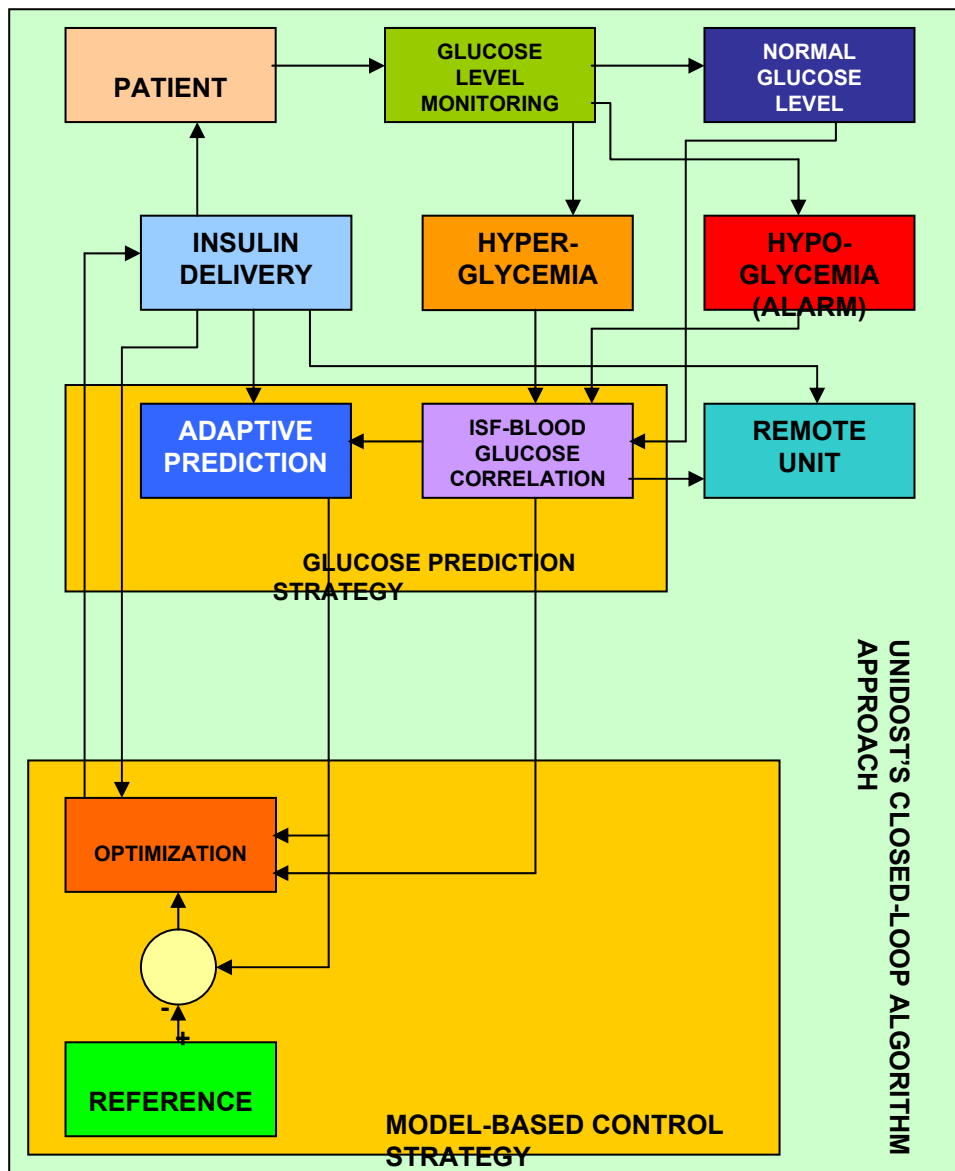
# CONVENTIONAL DIABETES THERAPY APPROACH



# MONGOOSE APPROACH



# MONGOOSE APPROACH



## OUR SUPERIORITY AND ADVANTAGES

Fully automated closed-loop glycemic control !!!

Polymer-based MEMS technology – cheap mass production !!!

Inexpensive device – partially disposable – minimally invasive !!!

Considering both type 1 and insulin-treated type 2 patients.

Imprecision of < 4% for glucose measurements !!!

**We introduce new concepts for insulin therapy initialization and adjustment, i.e. make a completely new modeling of the patient and base the decision algorithm on that – Our system mimics the person-specific natural plasma profile of endogenously secreted insulin !!!**

**With our unique technology, we are able to monitor the glucose level continuously in the real sense meaning that the monitoring interval can be a few seconds, which can be fully controlled and adjusted !!!**

**Our unique technology enables us to place the micro glucose sensor out of the subcutaneous space, i.e. outside the body eliminating the effects of implantation site specifics like tissue glucose utilization, local tissue reactions, blood flow, etc. !!!**

**Safety issues and several challenges are carefully considered and addressed !!!**

**Integration with a remote control center !!!**

## **SOLUTIONS ARE ALREADY FOUND FOR THE FOLLOWING POSSIBLE CHALLENGES**

Allergic reactions or skin irritation.

Huge resistance or counter-pressure of the epidermis layer of the skin applied on the microneedle array, and break of microneedles.

Device shut off during the replacement of the disposable part of the MEMS unit.

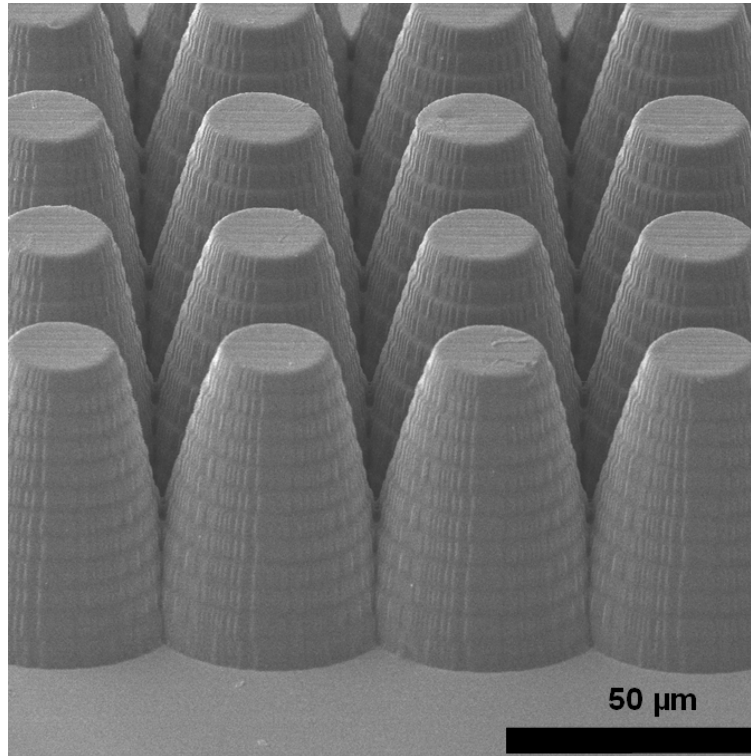
Unacceptably long lag time between the interstitial glucose level and the blood glucose level.

The microreservoir opens partially or spontaneously.

The microreservoir does not open when necessary.

Insulin does not diffuse or dissolve, although the microreservoir opens.

## EXAMPLES TO CURRENT CAPABILITIES AS A CONSORTIUM



Array of needle-like structures of SU-8 photoresist produced by multiphoton effect.

These structures are not hollow and are actually not used as needles but for a different purpose, which will not be revealed here.

## EXAMPLES TO CURRENT CAPABILITIES AS A CONSORTIUM



Biocompatible drug flow sensor on a 1 EURO coin. Sensor range: 50  $\mu$ l/h.