ACCuracy OF the RISK

NON-INVASIVE GLUCOSE METER

A REVOLUTION IN NON-INVASIVE DIABETES MANAGEMENT

Accofrisk™ is an affordable, non-invasive, wireless, glucose-sensing platform. Our revolutionary technology enables people with diabetes to accurately monitor their blood glucose levels for better management of their condition.

The glucose readings can be taken occasionally or continually throughout the day and results are instantly displayed on the device or can be transmitted via Bluetooth to a mobile app, where the user can manage the data and receive alerts.

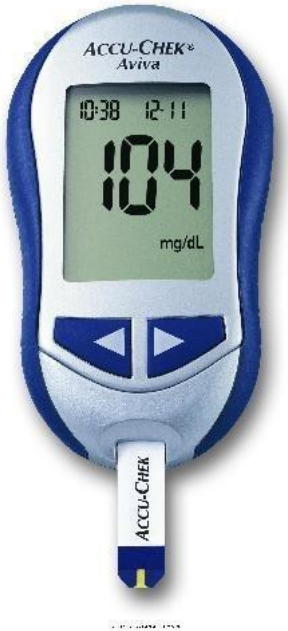
Diabetes is a worldwide global challenge.

Diabetes Mellitus is a chronic disease characterized by an acute lack of the hormone insulin. Diabetes leads to metabolic disorders, as well as to an increase in blood glucose and sugar levels.

Nowadays around 463 million people all over the world suffer from diabetes, which is 6,028 % of the total population of the planet. According to the statistics, the prevalence of diabetes is growing every year. "**The Nation**" estimates that by 2030, diabetes will cause one in seven deaths on the planet.

Diabetes and its complications, societal costs, and deaths have a huge and rapidly growing impact across the globe. In 2019: approximate 463 million adults (20-79 years) were living with diabetes and by 2045, this is expected to rise to 700 million. 79% of adults with diabetes were living in low- and middle-income countries Diabetes caused 4.2 million deaths. (*https://www.reportsanddata.com/report-detail/insulin-market*)

The global type 2 diabetes market is set to almost double from $31.2 billion in 2015 to $58.7 billion by 2025, representing a compound annual growth rate of 6.5%, according to research and consulting firm GlobalData. (https://drug-dev.com/global-type-2-diabetes-market-set-to-almost-double-to-58-7-billion/)



It is very important to monitor your sugar level with a glucose meter for all patients with diabetes or hypoglycemia. It is a small computerized device that measures and displays your blood sugar level. A glucose meter is one of the most effective tools for controlling the course of the disease.

Basically, all blood glucose meters are the same. You insert the test strip into the device. Then prick your finger with a needle or lancet and place a drop of your blood on this strip and wait for the readings to appear on the screen. The main differences are in the price, memory capacity of such devices, measurement accuracy (this is important when determining the dose of insulin) and the length of testing time. New systems have recently begun to appear that are somewhat different from all the others. They are based on the principles of **Raman spectroscopy** and **Photoplethysmogram**.

NEW DEVICES FOR MEASURING SUGAR LEVELS IN THE BLOOD.

iQuickIt Saliva Analyzer - is a blood glucose meter that detects blood sugar levels not by blood analysis, but by monitoring saliva. The developers of this device, which works in conjunction with a smartphone, set out to reduce the pain during measurements. The blood glucose meter is not sold yet and is being tested. What differs the device is that it allows you to measure not only the level of sugar but also the level of acetone in the saliva of diabetics. Acetone appears in the saliva of diabetics when the disease is in the acute stage, in diabetic ketoacidosis, which can be fatal. However, if for example, the sugar level is 550 and the saliva analysis shows the presence of acetone, the mobile device that received the data from the analyzer will send a message to the patient to immediately seek medical help, and the same message is sent to the patient's relatives and/or the attending physician.

SUGARSENZ.

(https://glucovation.com/)

The California-based company Glucovation has developed a system for continuous monitoring of blood sugar SugarSenz, which can be used by both diabetics and healthy people. Like some other similar systems for diabetics, the device is attached (glued) to the skin and periodically penetrates the skin independently and painlessly to obtain a blood sample for measurement. According to the developers, the system does not require calibration using blood from a finger. Sugar levels are measured electrochemically using a technology developed at Glucovation. The sensor can work for 7 days without interruption and transmit statistics to a smartphone

or physical activity tracker every 5 minutes, allowing you to get real-time analysis of how diet or exercise affect your metabolism. In this case, complex metabolic data is converted in the application into metrics that are understandable to the user.

GLYSENS.

(http://glysens.com/)

GlySens has developed an implantable glucose monitoring system that can work for about a year without requiring replacement. The system consists of two parts. One is a sensor that is similar to a milk bottle cap, only thinner, which is implanted under the skin in the fat layer. It connects wirelessly to the second part - an external receiver that is slightly thicker than a mobile phone. The receiver shows the current glucose level, the latest historical data, trends, and gives warning signals when the set blood sugar level is exceeded. It is assumed that in the future the receiver will be replaced by an application running on a mobile phone. The design of the system resembles similar subcutaneous systems that are already available on the market (DexCom, Medtronic, Abbott). The fundamental difference is that sensors in existing systems need to be recalibrated several times a day and can remain in place for no more than a week. Unlike competitive systems, the GlySens sensor tracks oxygen levels, which gives it its unique stability. Glucose and oxygen pass from the bloodstream to the membrane that covers the matrix of electrochemical detectors. The membrane is coated with an enzyme that interacts with oxygen. By measuring the amount of oxygen remaining after the reaction with the enzyme, the device can calculate the degree of the enzymatic reaction and, consequently, the glucose concentration.

SOCRATES COMPANION.

(https://socrateshealthsolutions.com/)

Socrates Companion is fundamentally different from its counterparts - it is a non-invasive blood glucose meter. However, it still exists in the form of a working prototype, and to obtain one, many people who have long been hungry for such a device will have to wait a little longer. The developers of the device were able to create a completely new technology for measuring sugar levels - without using the painful injection necessary for blood sampling. By simply attaching the sensor to your ear, the user can get an accurate analysis of the sugar content in a few seconds. The search for the possibility of measuring the level of sugar in the body in a non-invasive way has been going on for about 20 years and so far all attempts have failed, because the accuracy of measurements left much to be desired. According to the company, the patented technology used in Socrates Companion has solved this problem.

DEXCOM.

(https://www.dexcom.com/)

The American company Dexcom has updated its Dexcom G4 PLATINUM glucose meter, implementing a simulation of the pancreas in its software algorithm (in terms of measuring glucose levels). This made it possible to achieve almost laboratory accuracy of measurements. Dexcom G4 PLATINUM glucose meter allows you to measure glucose

levels continuously 24/7. Such a device doesn’t require piercing your finger every day. Its sensor patch is installed in the area of the abdomen and every 5 minutes transmits the measurement results to a gadget similar to an MP3 player. This gadget not only displays a graph of changes in the amount of sugar in the blood but also warns the carrier when this indicator goes out of the norm. You can also sync statistics with the mobile app for smartphones. Continuous monitoring of glucose levels allows you to identify factors that affect it and optimize the treatment of a diabetic patient (you will need an additional device to take data from the sensor).

SugarBEAT.

(**https://sugarbeat.com/**)

The British company Nemaura is preparing to launch its non-invasive glucose meter SugarBEAT. It is glued to the skin and transmits measurements (every 5 minutes) directly to the smartphone. You need to glue it every day (removing it at night) so that the patch with micro-needles is fresh. But the device itself can work for several years without replacement. This will be the first glucose meter that people can use just for the sake of fitness or out of interest in their glucose levels because it doesn't hurt to glue it at all. If you have diabetes, then for the accuracy of changes, you need to calibrate the device by first measuring the glucose level with a regular glucose meter. The exact cost of SugarBEAT is not yet known, but Nemaura says it will be comparable to the cost of conventional blood glucose meters and test strips.

EVERSENSE.

(https://www.eversensediabetes.com/)

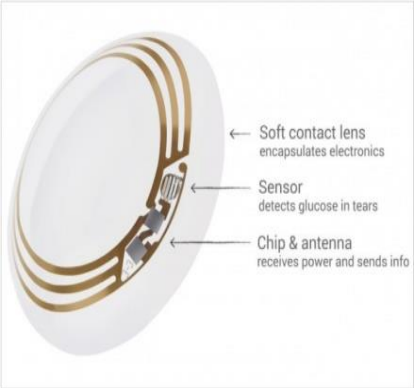
Modern sensors for continuous glucose monitoring (such as FreeStyle Libre) are certainly more convenient than daily finger punctures, but they still need to be replaced weekly. The American company Senseonics has created the Eversense sensor, which works without replacement for 3 months. However, it is difficult to install it - you need (in the clinic) to implant the sensor under the skin (in the shoulder area) and paste the transmitter over it on the skin. The transmitter receives measurements from the sensor and transmits them to the smartphone, where they are recorded in the app, and if necessary, the app reports dangerous glucose levels.

FreeStyle Libre.

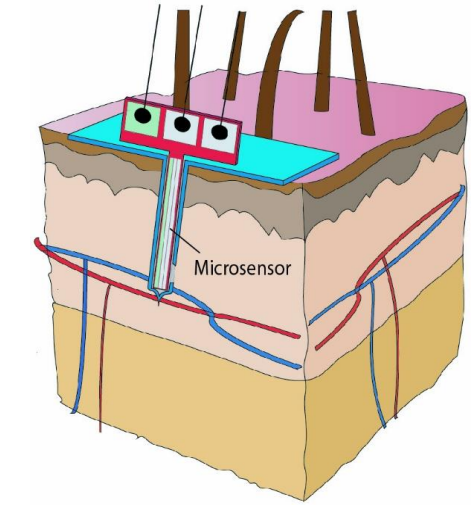
(https://www.freestylelibre.us/)

Gadget FreeStyle Libre (American Corporation Abbott) does not save a person from punctures at all. Moreover, it makes a puncture every minute. However, with the help of an ultra-thin thread that moves no further than the subcutaneous layer the person does not feel anything. This measuring element is located inside a waterproof sensor that is attached to the back of the forearm. The second component of the blood glucose meter is a special device that reads and displays the sensor readings. The blood glucose meter continuously monitors the level of glucose in the blood. Measurement results are stored on the device for up to 90 days, so the user can view their statistics for a long time.

GOOGLE CONTACT LENS.



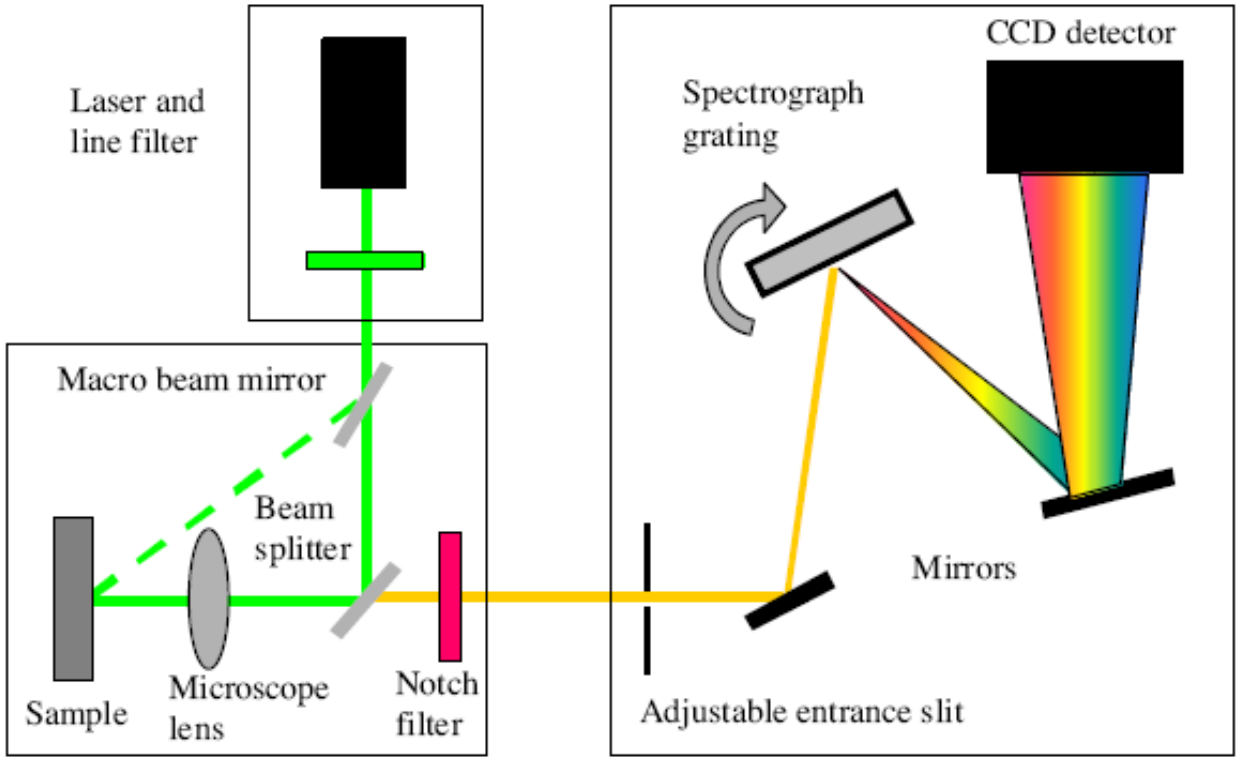
The secret Google X laboratory (which implements all sorts of crazy ideas of Seryozha Brin, such as Google Glass smart glasses) has introduced contact lenses that can send all blood glucose meters to the landfill, and most importantly - strips for blood glucose meters, with which people with diabetes pierce their fingers. These contact lenses use a special sensor to measure glucose levels not in the blood, but tears. Moreover, they can do this constantly (monitor glucose levels), and not just a couple of times a day. Besides, the developers are going to embed a led in the lens that will warn a person when a dangerous glucose level is reached. The lenses will be able to transmit data to the smartphone so that the doctor can see the dynamics of the patient's recovery.

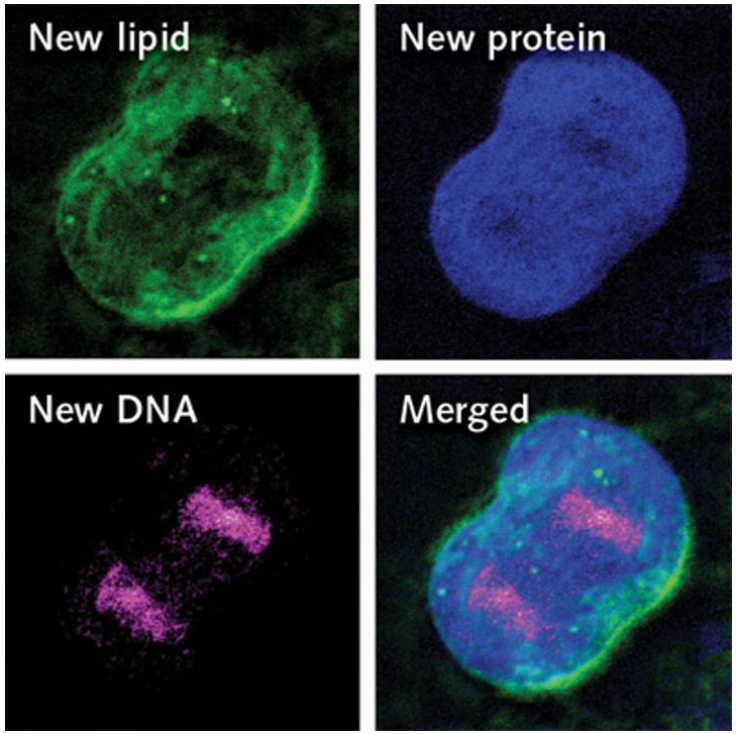


BLOOD GLUCOSE METER IN THE FORM OF A PATCH.

Plasters (patches) with microneedles will soon be used instead of injections for delivering drugs. But it turns out that this technology can also be used to measure the blood glucose. Scientists from the Institute of Technology in Stockholm have created (and already tested) a prototype of such a patch. Its needles are 50 times smaller than those used in modern blood glucose meters, so when sticking such a patch on your hand, you will feel it just like a regular patch. Measurements from the patch will be sent directly to your smartphone.

RAMAN SPECTROSCOPY.





Raman spectroscopy is a class of analytical techniques based on the collection and analysis of inelastically scattered light that contains information about the vibrational modes of a sample's constituent molecules. Different variants of Raman spectroscopy have been applied to the study of blood, and each has its own advantages and disadvantages.

GlucoBeam, RSPSystems, Denmark.

https://www.rspsystems.com/

As of 2017, the original idea to non-invasively glucose monitor using Raman spectroscopy became highly within reach, since the technology had matured enough to lead to the design of the first prototype to be used in trials for market approval in Europe.

Early 2020 RSP Systems was granted the European Patent Certificate covering our Critical Depth Technology, supplementing our existing US patent.

DiaMonTech, Berlin.

https://www.diamontech.de/home

AN AWARD WINNING PROJECT
In June 2017, DiaMonTech won a prestigious award for “most innovative German startup” from German business magazine Bilanz.

Shoebox-sized device to be used as a prototype to conduct human trials with our technology.

2023/24 Wearable device that continuously measures blood glucose.

PHOTOPLETHYSMOGRAM.

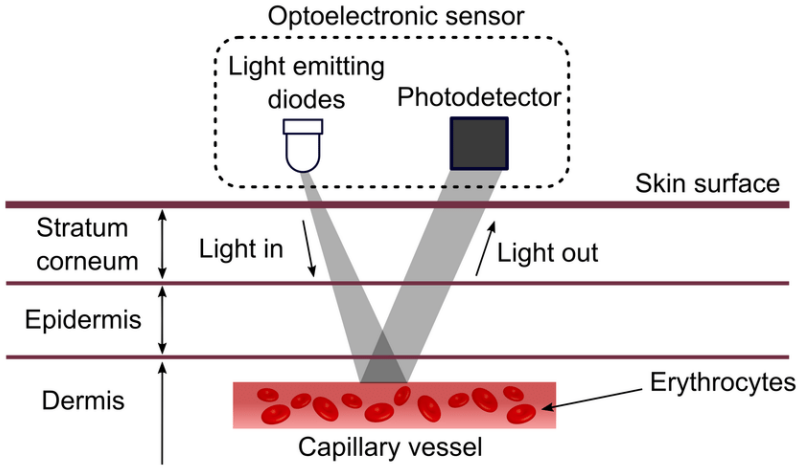
CNOGA, Combo Glucometer, Israel.

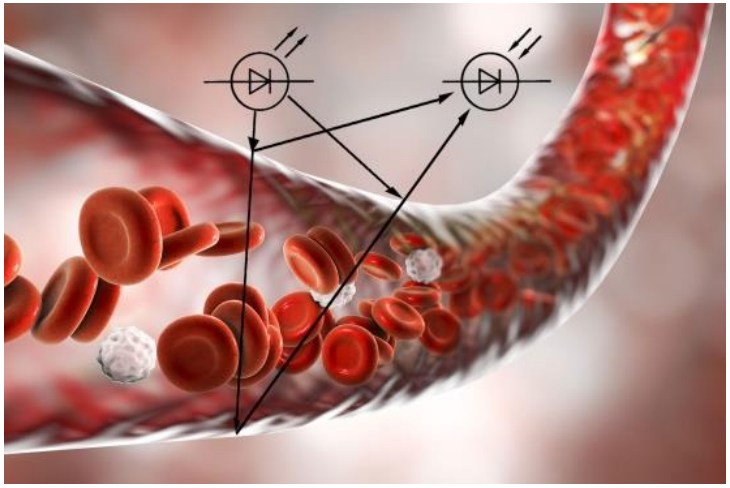
https://cnogacare.co/

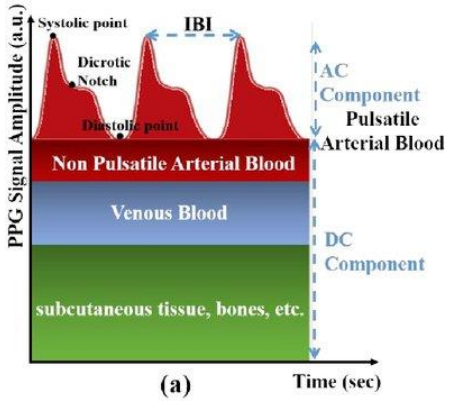
CnogaCare is a leading Digital Healthcare company which develops complete end to end solution for Remote Patients Monitoring integrating innovative Noninvasive Medical Devices and Digital platforms.

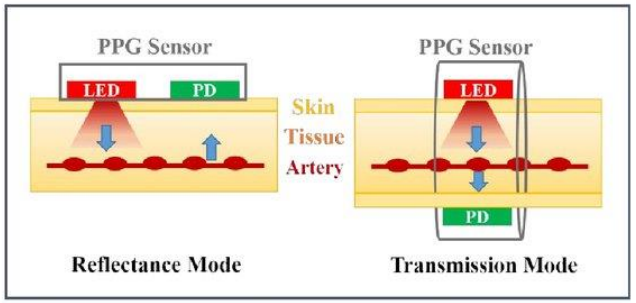
PHOTOPLETHYSMOGRAM.

We take a band device for measuring the heart rate (HR – heart rate) as a basis. This device is equipped with a led (a light-emitting diode) that emits monochrome coherent light radiation in a narrow frequency range. Pulse measurement is based on the reception of radiation reflected by a photodiode from subcutaneous capillaries, which changes synchronously with the pulse. When the capillary is full, it almost completely absorbs the light; when it is not full, it slightly absorbs the light.









The principle of heart rate measurement used in "smart" bands differs from what is used in conventional medical devices with mechanical or electrical action. This is due to the sensors built into the inner side of the bracelet. The method of photoplethysmography is used for their work, which allows you to determine changes in blood volume using optical radiation. When contracting, the heart muscle provokes an increase in blood pressure. Capillary blood flow increases, resulting in more light being absorbed. The sensor registers this, and by counting the number of such surges per minute, the device determines the heart rate.

Photoplethysmogram is a method for recording blood flow using an infrared or light emission and a photoresistor or phototransistor. The greater the blood flow, the more light is absorbed by erythrocytes in the body's tissues, so less light comes to the photoresistor.

The speed of blood flow in capillaries is low and amounts to 0.5-1 mm/s. Thus, each blood particle is located in the capillary for about 1 second. The Small thickness of the blood layer (7-8 microns) and its close contact with the cells of organs and tissues, as well as the continuous change of blood in the capillaries, make it possible to exchange substances between blood and tissue (intercellular) fluid.

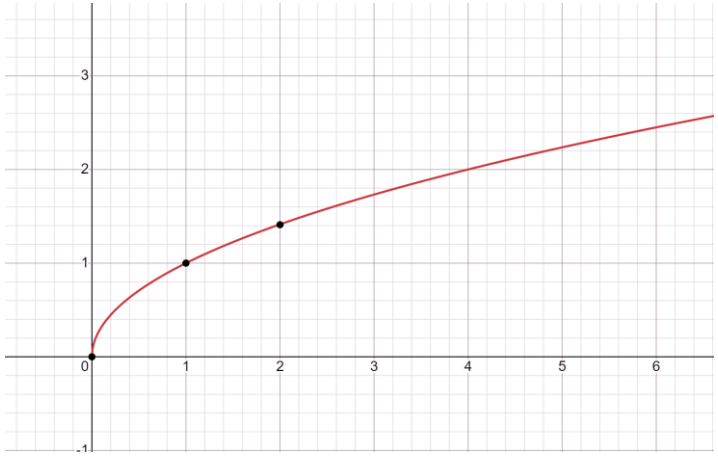
Photoplethysmogram allows you to measure the volume pulse of blood caused by periodic changes in blood volume with each heartbeat, heart rate, and variability of heart rate.

By using a fine spectrum analysis **photoplethysmogram** will allow you to find out the percentage of glycated haemoglobin since glycated erythrocytes absorb light differently than the common ones.

MATHEMATICS.

Diabetes mellitus is characterized by the fact that glucose when changing its shape, accumulates in the cell. When sugar accumulates in the cells, the water content in the blood increases, which affects the viscosity of the blood, the speed of blood movement in the capillaries and its colour, making the blood lighter and more fluid. In this case, the relative increase in blood flow rate is proportional to the square root of the relative increase in glucose concentration (the flow rate formula for Newtonian fluid).

$$y = \sqrt{x}$$



For a specific person, the speed function changes the form:

$$V = V0 + C\sqrt{g}$$

V - the speed; V0 - the initial speed; C – the personal coefficient; g - the sugar content.

The Doppler effect is used to measure the speed of blood flow when a moving medium changes the frequency of the reflected signal. Thus, we measure the speed of blood flow and can determine the change in sugar levels (increase or decrease depending on the speed of blood flow).

The Doppler Effect is that an object in motion changes the frequency of the signal reflected from it or emitted by it. When the blood cell tends towards the emitter it means that the reflected frequency is higher, if it moves from the emitter - the reflected frequency is lower.

The device measures the Doppler frequency shift:

$$\Delta F=(Fs-Fr),$$

Fs – the frequency of the sensor (led), Fr – the reflected frequency.

The lightwave lies on the velocity vector at an angle α. ΔF is determined by the projection of the velocity vector on the light beam (V·cosα):

$$\Delta F=2Fs\cdot V\cdot \cos\alpha/C,$$

C - the speed of light in the body tissues.

For the evaluation of blood flow velocity they use the Doppler equation:

$$V=\Delta F\cdot C/2Fs\cdot \cos\alpha.$$

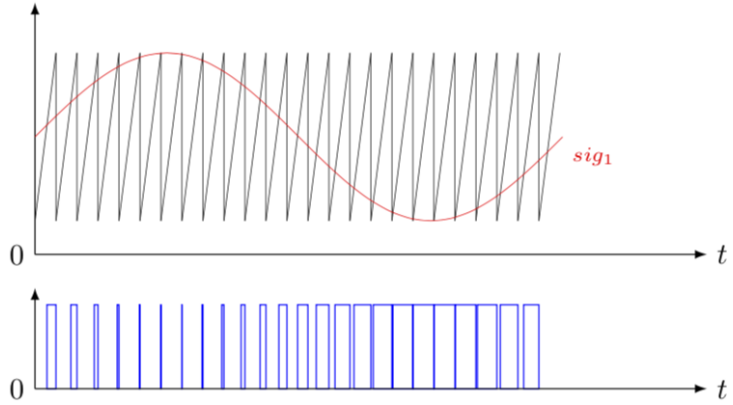
In order to acquire an accurate result, you need to know the initial glucose level (determined once by a classic blood sugar test).

Compared to other methods of non-invasive glucose assessment, this method allows you to quickly assess the patient's condition, to perform diagnostics and to monitor blood glucose levels, as well as to make recommendations for eliminating identified problems in real-time. At the same time, a fully operational, reasonable and documented conclusion is made about the patient's condition, which may be important for medical insurance. The method of measuring the Doppler frequency shift reduces

external interference and measurement errors. It does not require any additional complex devices for assessing glucose levels, as well as piercing the patient's skin and attaching sensors to the body. The device is convenient for the patient, allows you to assess glucose levels several times a minute, and to detect a sharp increase or fall in glucose levels.

OPERATION ALGORITHM.

1. More than 50 complex set pulses per second are formed on the Led of the band (for example, analogues of delta functions, sawtooth and reverse sawtooth signals). The device also receives the high-accurate response from blood vessels on a single time scale (photo location).



2. The received signal is promptly treated by means of the band and hazardous events are highlighted, for example, changes in blood density, its density (at the minimum and maximum of the absorbed signal), "colour" (changes in the absorption band relative to the main frequency of the photodiode radiation).

3. The received signal is transferred to a smartphone, where the Fourier transform is performed with the detection and correlation of the spectrums of the emitted (item 1) and the received signal (several tens of harmonics).

4. The "capillary model" is being created and its changes are being monitored. The capillary model is an operator for changing the spectrum of a light signal when light passes through a vessel. Practically we consider the capillary as a dynamic optical filter and associate its parameters with the parameters of the blood flowing through it.

5. We calibrate using external parameters (a certain set of parameters corresponds to a certain sugar level, haemoglobin level, etc.).

6. The display of sugar and haemoglobin parameters after the calibration on the band is continuous.

7. We calculate the level of glycated haemoglobin.

Currently, the number of people diagnosed with diabetes in the UK is estimated to be 3.5 million.
It is predicted that up to 549,000 people in the UK have diabetes that is yet to be diagnosed. This means that, including the number of undiagnosed people, there is estimated to be over 4 million people living with diabetes in the UK at present.
This represents 6% of the UK population or 1 in every 16 people having diabetes (diagnosed and undiagnosed).
(https://www.diabetes.co.uk/diabetes-prevalence.html)

Prediabetes is a serious health condition where blood sugar levels are higher than normal, but not high enough yet to be diagnosed as type 2 diabetes. Approximately 88 million American adults—more than 1 in 3—have prediabetes. Of those with prediabetes, more than 84% don't know they have it. Prediabetes puts you at increased risk of developing type 2 diabetes, heart disease, and stroke. Race and ethnicity are also a factor: African Americans, Hispanic/Latino Americans, American Indians, Pacific Islanders, and some Asian Americans are at higher risk.
(https://www.cdc.gov/diabetes/basics/prediabetes.html)

According to analysis, digital diabetes global market expected to reach $16,329.6 million by 2026 growing at a high single digit CAGR from 2019 to 2026.

(https://www.prnewswire.com/news-releases/global-digital-diabetes-market-outlook-to-2026-a-16-billion-industry-opportunity-300980794.html)

New findings from Juniper Research reveal that wearables, including health trackers and remote patient monitoring devices, are set to become 'must haves' in delivering healthcare, with $20 billion forecast to be spent annually on these devices by 2023. Meanwhile, assistive hearables, or connected hearing aids made available via healthcare providers, as well as directly to customers at varying price models, will mean this sector generates revenues of over $40 billion by 2022.

(https://www.juniperresearch.com/press/press-releases/healthcare-spend-in-wearables-reach-60-bn-2023)

The US digital health sector enjoyed its second-highest year of investment in 2019, just slightly down on an all-time record in 2018.
A total of $7.5bn (£5.7bn) was invested into a diverse range of start-ups attempting to digitise and disrupt the colossal $3.8 trillion (£2.9 trillion) US healthcare system, and overhaul a healthcare system that continues to provide some of the best care on the planet, yet is one of the poorest in equity among Organisation for Economic Co-operation and Development (OECD) members.

(https://www.digitalhealth.net/2020/01/ces-2020-digital-health-investment-2019/)

The Europe diabetes devices market size was valued at USD 6.4 billion in 2018 and is projected to grow at a CAGR of 4.0% over the forecast period. The demand for diabetes devices is on a rise owing to the increasing incidence of diabetes due to sedentary lifestyle, obesity, and unhealthy eating habits. Obesity is the primary driving factor responsible for causing diabetes among all age groups.

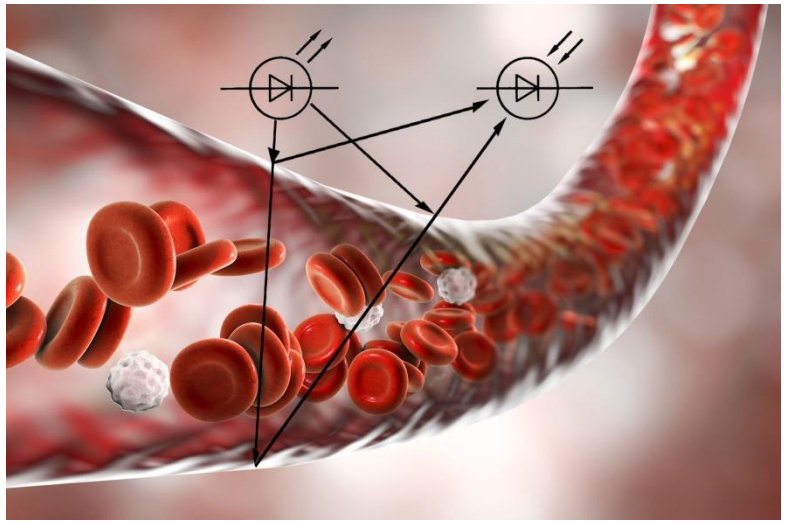
(https://www.grandviewresearch.com/industry-analysis/europe-diabetes-devices-market)

THE "NON-INVASIVE BLOOD GLUCOSE METER" PROJECT DEVELOPMENT

1. USING A REGULAR LED IN A FITNESS TRACKER.

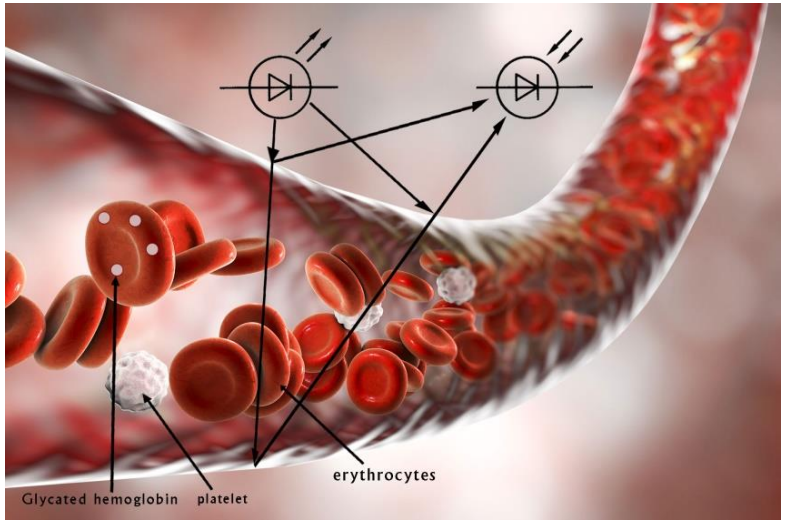
We capture the integral response which is the sum of reflections from all cells that were in the observed region of the capillary.

If there are multiple responses, we can solve the equation and find different blood parameters, but only from those that we have planned in advance.



2. USING A LASER IN A FITNESS TRACKER.

In the response, we will see the spectrum not only from blood cells (each gives a frequency maximum on a known wave) but also additional information that needs to be identified (for example, amoebas, nematodes, bacteria and bacterial clusters, Oncology (cell change) as well as an analysis of the lymphatic system).



3. DATA ACCUMULATION AND ANALYSIS.

For example, if something "new" appears in the blood:

a) there is a precedent for other patients (for example, pregnancy);

b) there is no precedent or if the saved blood data of a patient does not contain any data that was not there before, then the HEALTH platform is accessed where the data of other patients is stored, the data is verified and indications are given (tests>microscopy>new disease or pathology).

4. MEDICAL DATA COLLECTION - blood analysis, analysis of the lymphatic system generates the task of storing and processing an extremely large amount of data (approximately 5×10*8 bytes/day per person). Per 1 million patients it would be about ~5×10*14 bytes/day. This raises two challenges:

- reducing the amount of data;

- pre-processing of data for further rapid processing (search, diagnostics, comparison, forecast).

5. TREATMENT - floating-wavelength laser.

a) destruction of pathogen cells;

b) activation of neutrophils in the immune response.

It will take up to 7 months to develop, manufacture and test a prototype (at least 100 test subjects).

It will take 2-6 months to create patent applications.

It may take at least 6 months for the device’s expertise and certification (in Russia).

Make decisions based on fitness tracker data on the move. Our platform uses predictive algorithms and Artificial Intelligence to forecast and increase the accuracy of vital data that enhances positive behaviour and reduces the number of your appointments with any doctor.

www.accofrisk.com, E-mail: info@accofrisk.com