21AG-1C082

Լազերա-օպտիկական եղանակների կիրառումը բժշկական ախտորոշման սարքերի մշակման համար

Implementation of laser-optical techniques for development of medical diagnostic devices

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«Ամենամյա ամփոփիչ գիտաժողով 2025»

Դիլիջան, 5-10 հոկտեմբեր 2025

Project sub-tasks

I stage (3 years)

Development of a laser-optical imaging technique

Challenges and objectives

Challenges of efficient optical transmission imaging of thick highly scattering objects (notably biological organs)

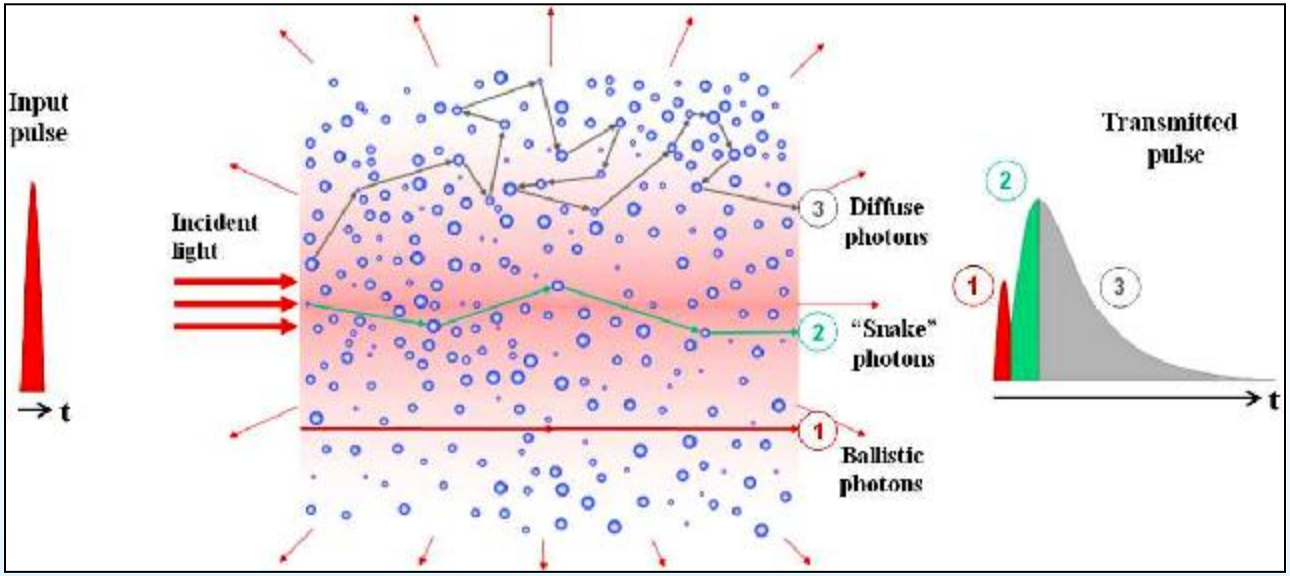
- Huge scattering. Diffuse scattering increases nearly exponentially with the sample thickness, making transmitted image unrecognizably blurred.
- Strong attenuation of direct light. Detection becomes complicated already for samples of several mm thickness.
- Big dynamic range of recorded signals. The signal amplitude can vary by several orders of magnitude for objects with variable thickness across the sample, making visualization difficult.

Challenges and objectives

The **objective** of this work was to develop and implement an optical transmission imaging device, which will provide:

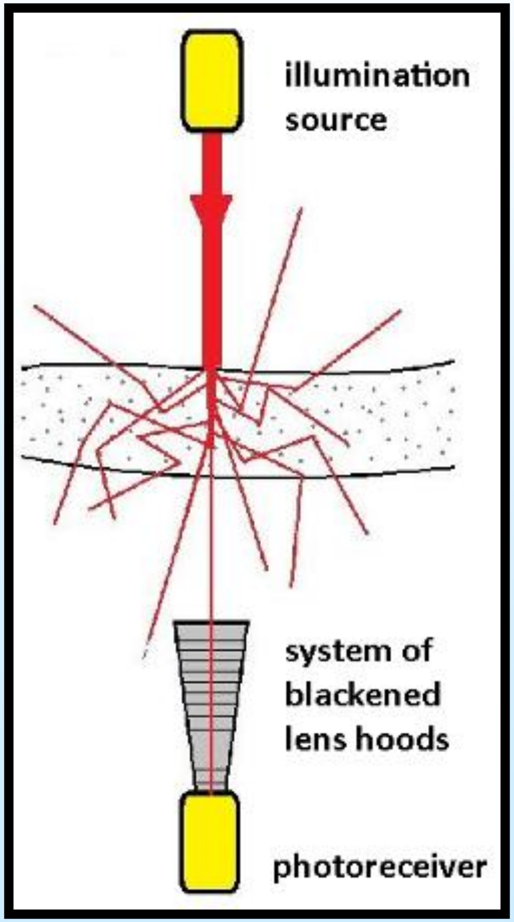
- Imaging of up to 30 mm-thick highly scattering objects, both with uniform and inhomogeneous thickness across the sample;
- At least 1 mm spatial resolution, independently of thickness across the sample;
- Uniformity of the image and high contrast, even for samples with variable thickness;
- Reasonable measurement time;
- Immunity against the external background illumination;
- Exclusion of necessity of the image processing software
- Low cost technological solutions.

Challenges and objectives



Temporal gating (filtering)

Selective detection of "ballistic" photons

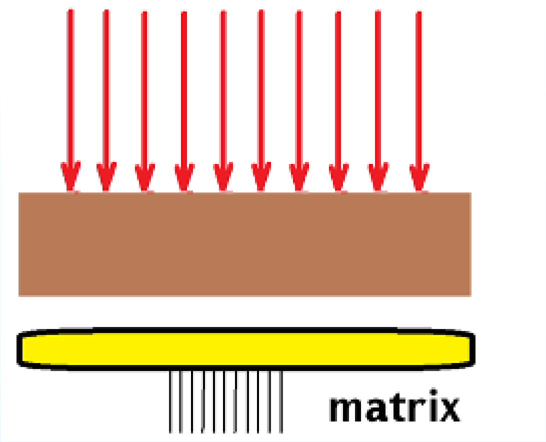


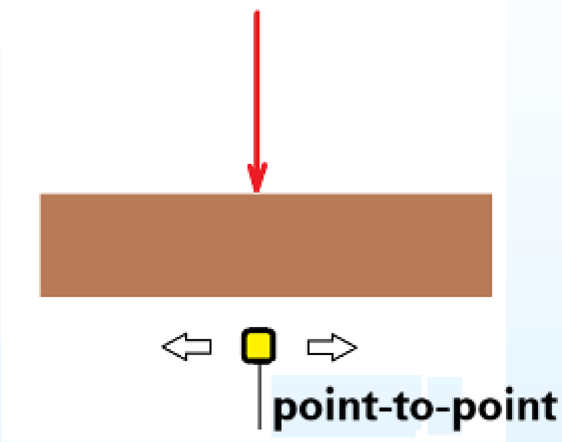
Spatial filtering

- ❑ Small detection solid angle is needed to block diffuse photons
- ❑ Highly-sensitive detection is required to record a negligible number of arriving ballistic photons, as the thickness increases to centimeter-scale

Challenges and objectives

Two imaging approaches: matrix vs point-to-point





2D recording (multipixel CCD, CMOS, photographic plate)

Direct recording of image

Low sensitivity

Complicated image hardware processing

0D recording (single-pixel scanned photoreceiver)

Rich possibilities of signal real-time hardware processing

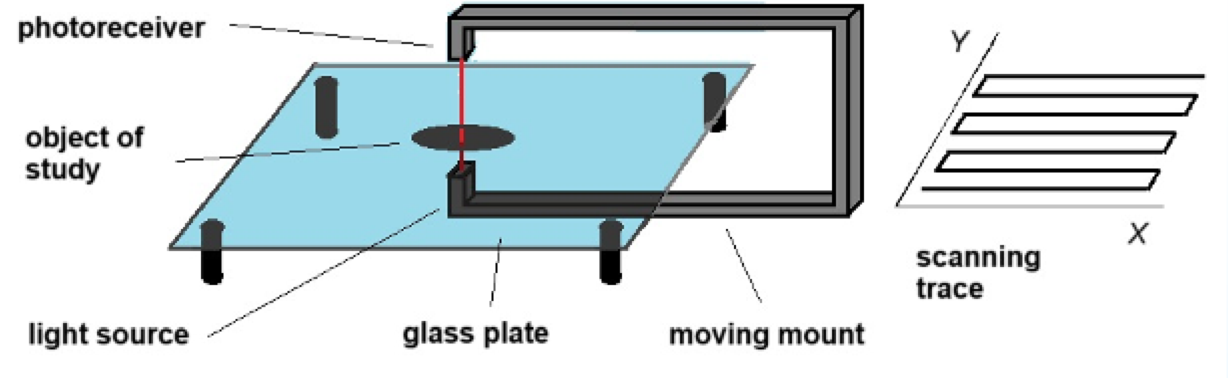
High sensitivity

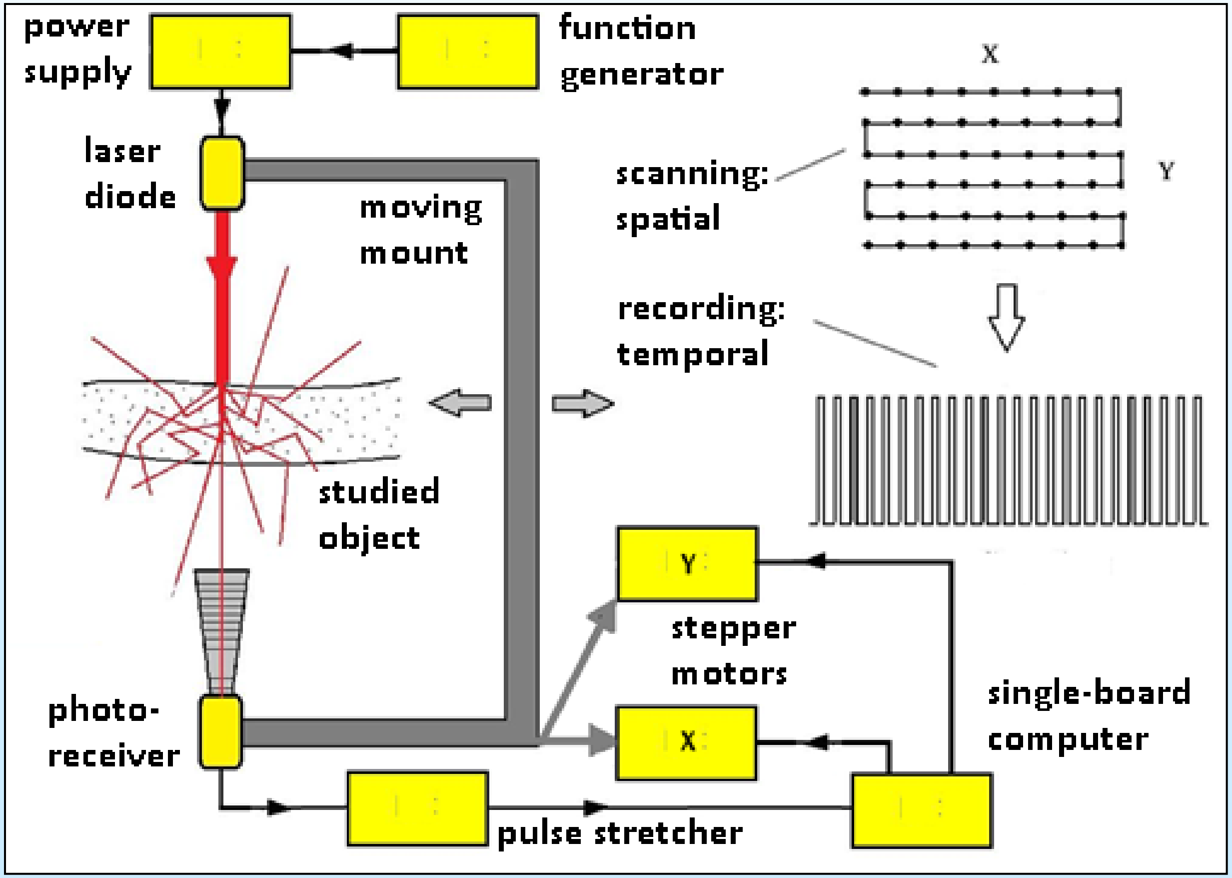
Slow recording, mechanical scanning

Experimental arrangement

Schematic diagram

Predominant detection of ballistic light





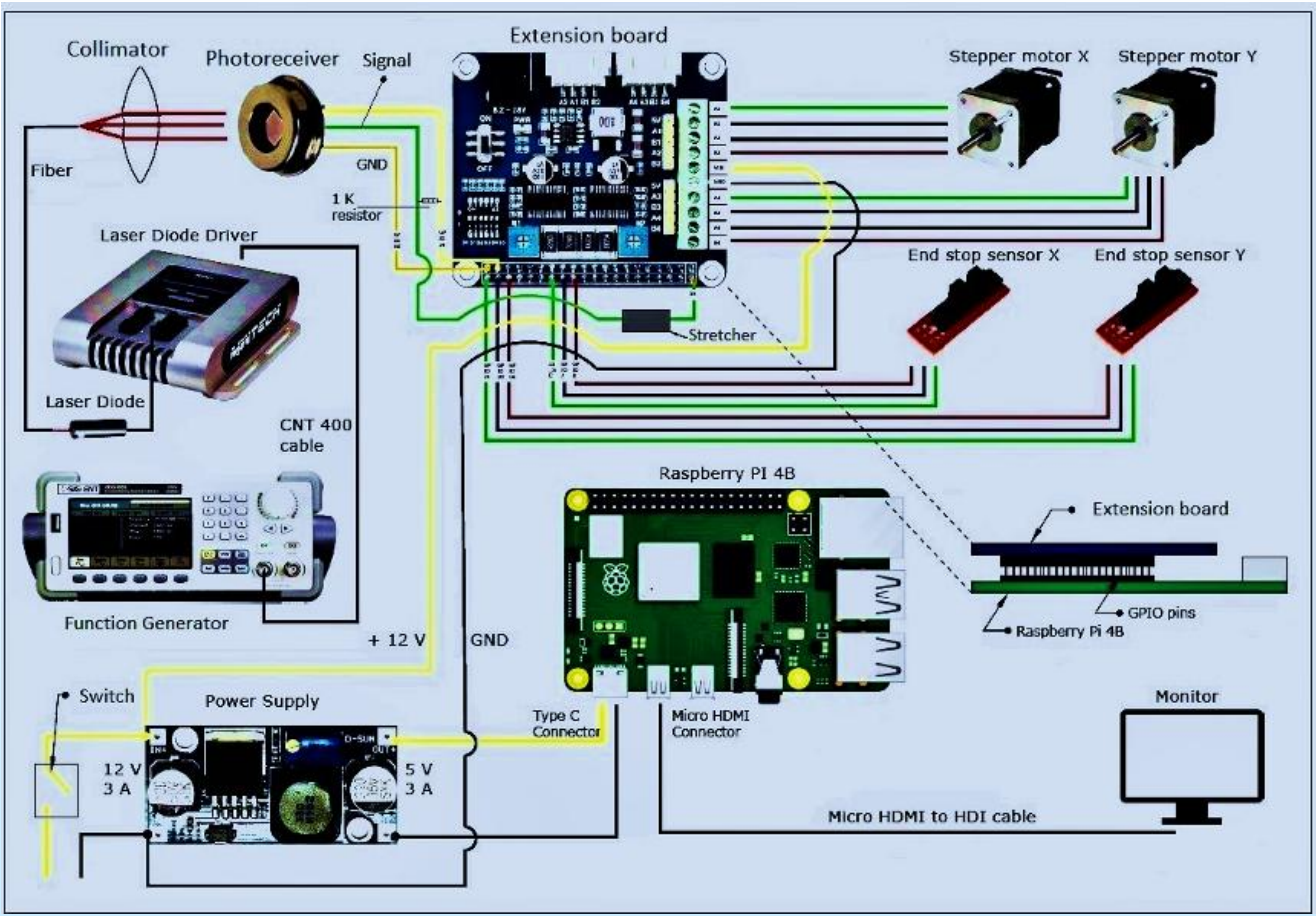
Scanning and recording are controlled by a Python code

Variable parameters:

- Starting point
- Scanning step (mm)
- Number of steps, by X and Y (max. 25 x 25 cm)
- Scanning speed (px/s)
- On-pixel data recording delay
- Grayscale color depth (linked with number of pulses per pixel)

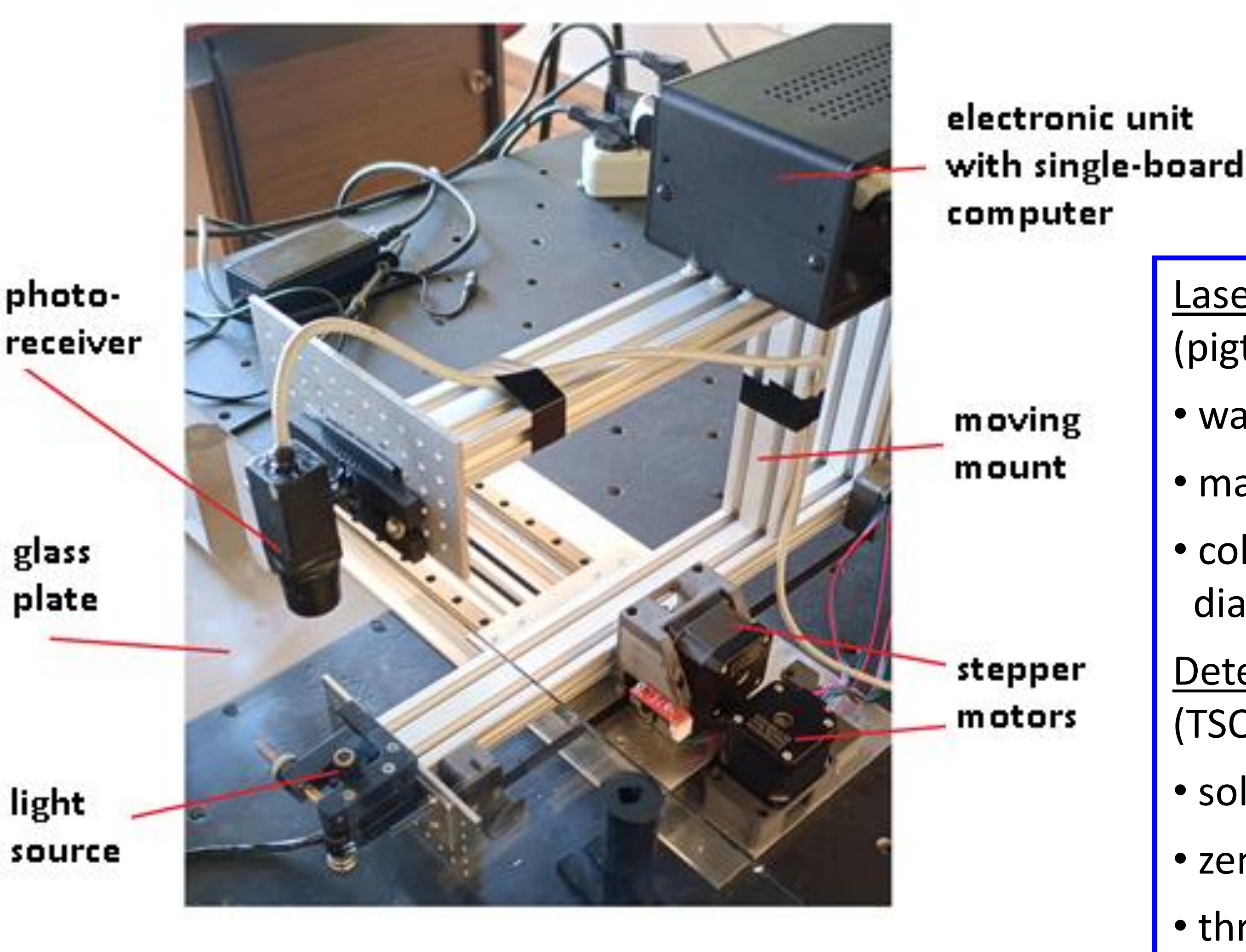
Experimental arrangement

Electronics



Experimental arrangement

Real appearance



<u>Laser</u>
(pigtailed butterfly LD)

- wavelength: 976.4 nm
- max. cw power: 650 mW
- collimated beam diameter: 1.5 mm

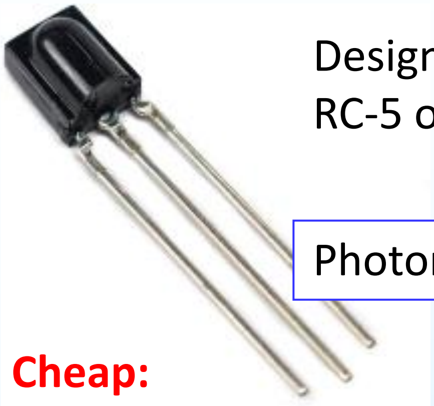
<u>Detection</u>
(TSOP photoreceiver)

- solid angle: 0.6 - 7 msr
- zenith angle: 0.8° – 2.7°
- threshold power: 0.1 nW

"Digital" detection of modulated (pulsed) light

Experimental arrangement

VS1838 infrared TSOP (thin small outline package) photoreceiver

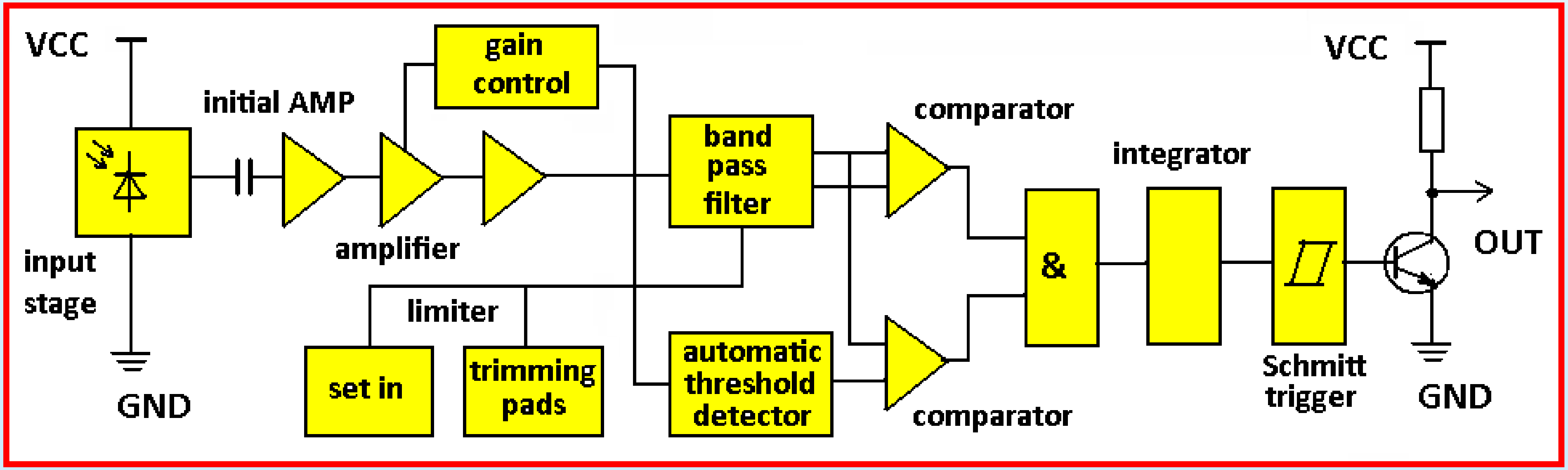


Photoreceiver

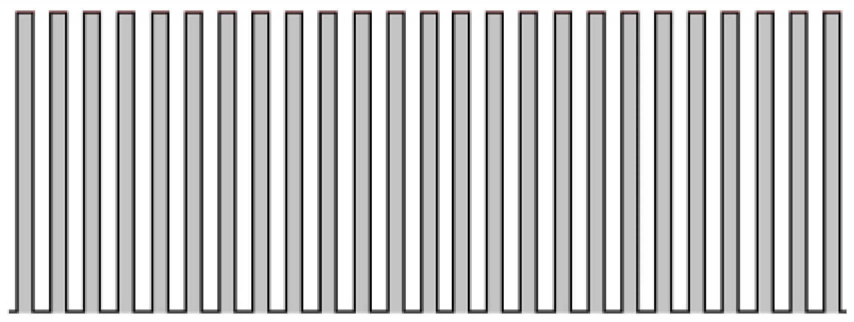
Designed for customer electronics infrared remote control, operated by RC-5 or NEC protocol: https://www.vishay.com/docs/80071/dataform.pdf

- Very low supply current; supply voltage: 2.5 V to 5.5 V
- PIN photodiode and preamplifier in one package
- Internal filter for PCM frequency
- Improved shielding against EMI
- Improved immunity against ambient light
- Insensitive to supply voltage ripple and noise
- TTL output: “1”- no signal detected, “0”- signal detected

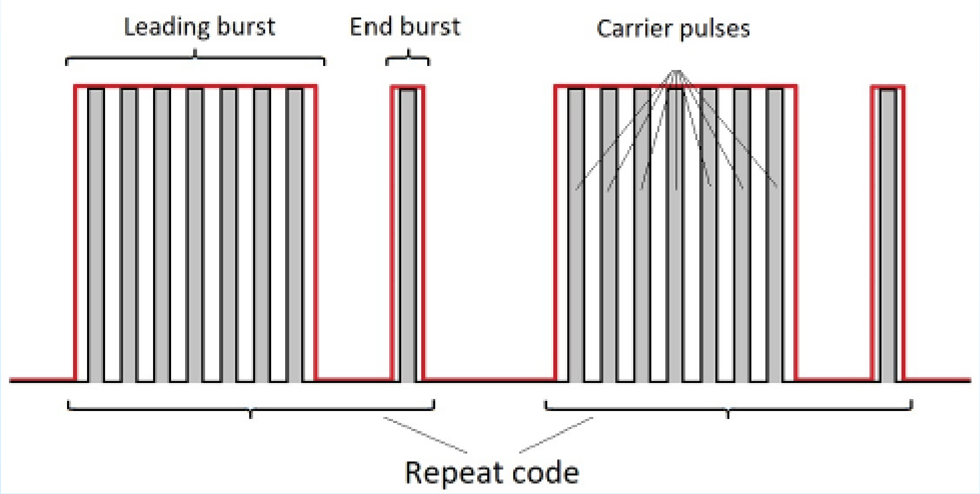
Cheap: all that just $0.7!!!



Experimental arrangement



38 kHz "carrier" modulation of input light



Envelope modulation of input light for the NEC repeat code

Other, customized envelope pulse sequences are also possible, respecting some requirements

Photoreceiver operation protocol: Forming a "proportional" image

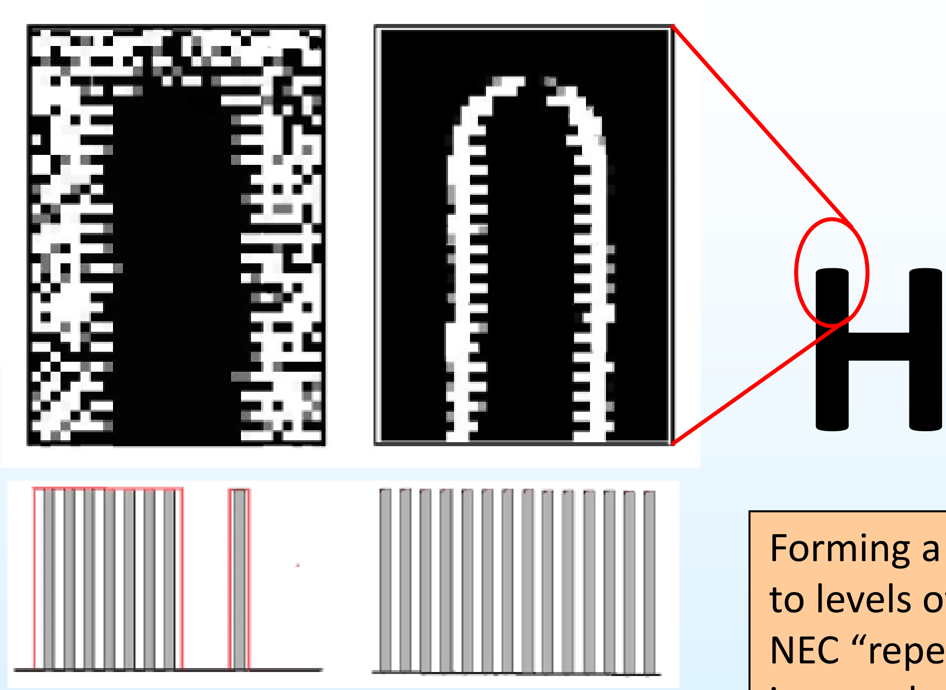
The photoreceiver works at 38 kHz rectangular "carrier" modulation with superimposed "envelope" (burst) modulation.

The NEC "repeat code"-type envelope modulation burst sequence:

1) 9 ms leading pulse burst;
2) 2.25 ms space;
3) 0.5625 ms pulse burst marking the end of the code;
4) 28.1875 ms space before the next leading pulse burst (reduced by 68 ms compared with original NEC protocol).

The envelope modulation frequency is 25 Hz (to synchronize the scanning speed with this code, the pixel-to-pixel time has to be ≈ 40 ms).

Scanning of planar scattering objects



Good model object for planar (uniform in thickness and composition) scattering: a stack of **white paper**; printed text models absorption

To visualize an absorbing feature with high contrast, it is expedient to employ a 2-level (black-and-white) scale instead of grayscale

Forming a **"proportional" image** (levels of gray correspond to levels of transmitted light):
NEC "repeat code" envelope modulation at 25 Hz frequency imposed on the 38 kHz rectangular carrier modulation of the laser radiation (**Left picture**)

Images of a fragment of the printed letter "H" covered with dozens of layers of white paper.

<u>Left panel</u>: image recorded with double (38 kHz carrier and 25 Hz envelope) NEC modulation;

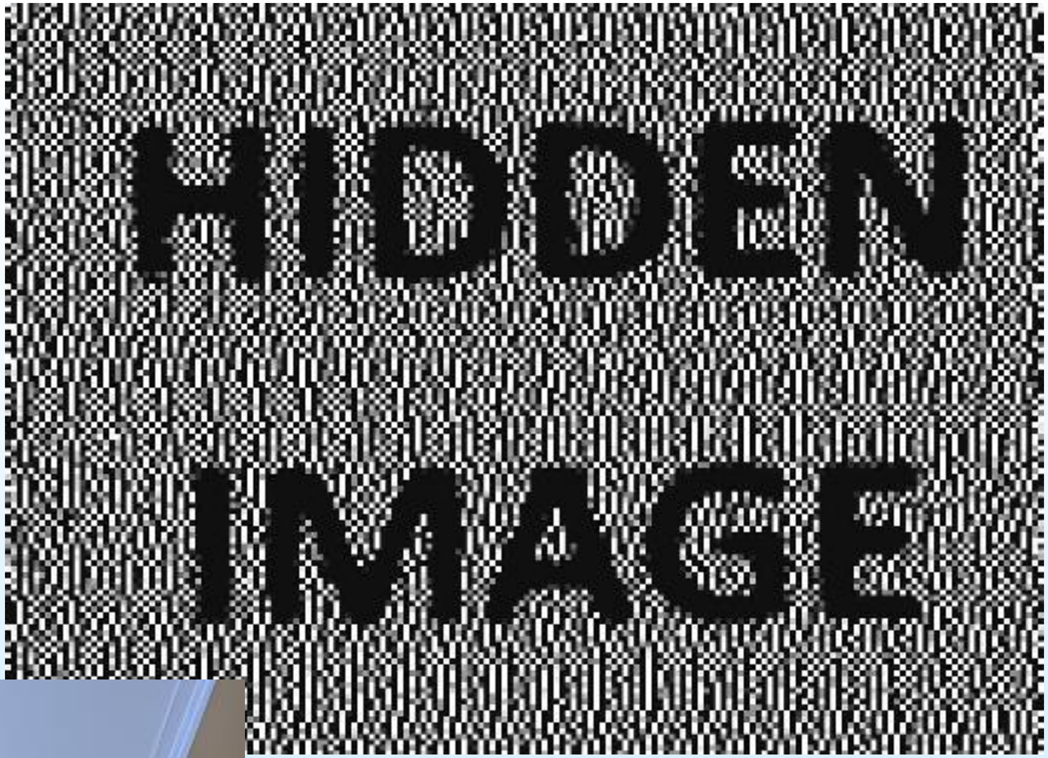
<u>Right panel</u>: image recorded with solely 38 kHz carrier modulation.

Forming an **"outline" (contour) image**: (highlighting edges of absorbing features):
Solely 38 kHz rectangular carrier modulation (**Right picture**)

TSOP is outright insensitive when the level of illumination is invariable in time. However, with the correct choice of scanning speed, a signal can appear when a sharp change in illumination level occurs between the neighboring pixels

Scanning of planar scattering objects

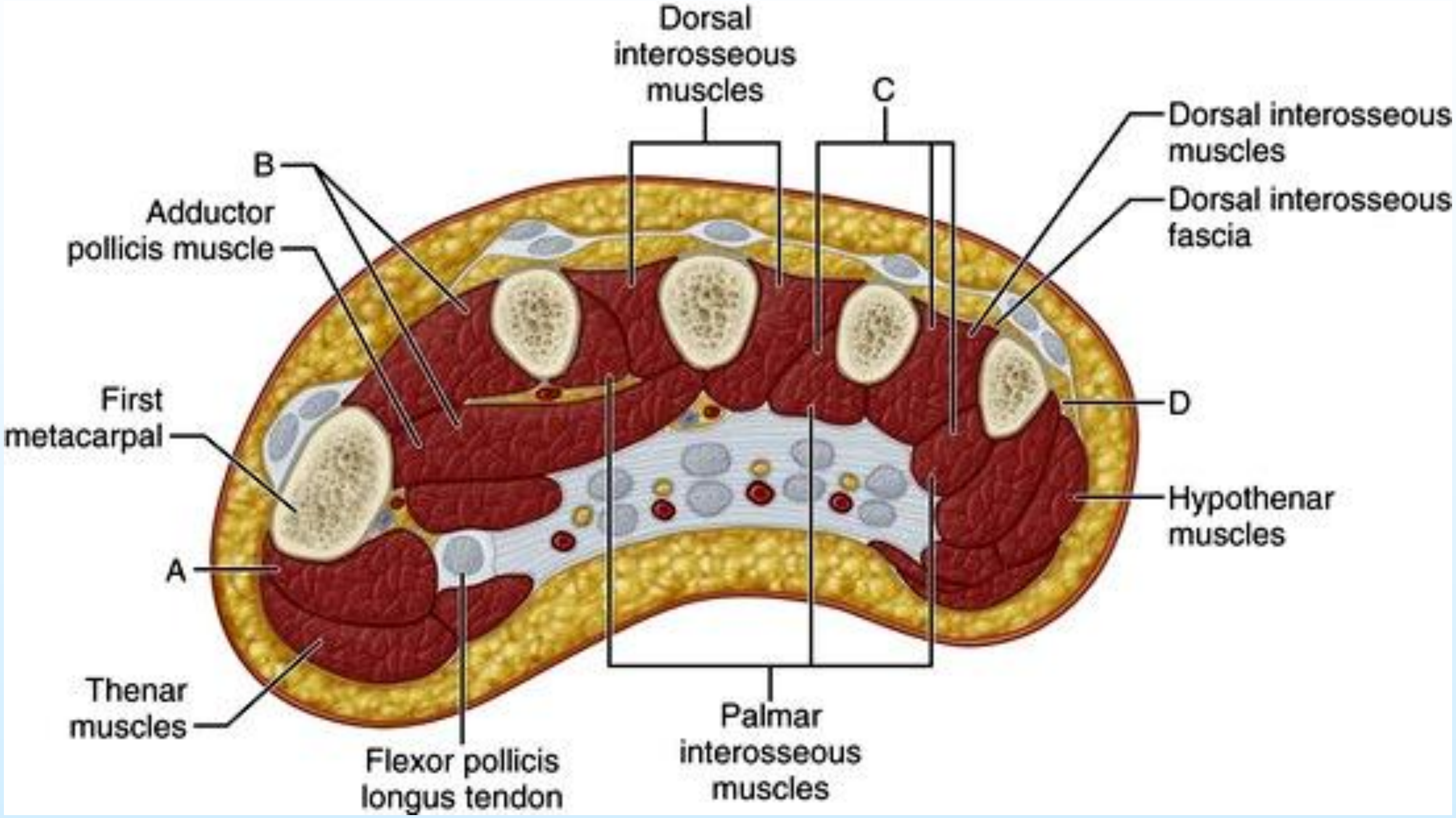
180 × 130 pixel transmission image of a text printed on A4 paper by a laser printer and sandwiched between 40 sheets of blank A4 paper of 80 g/m2 density



The scanning was done with double-modulated light source, 1 mm step, and pixel-to-pixel time of 12 ms (total recording time 4 minutes and 40 seconds).

Scanning of non-uniform bulk objects

Much more challenging task

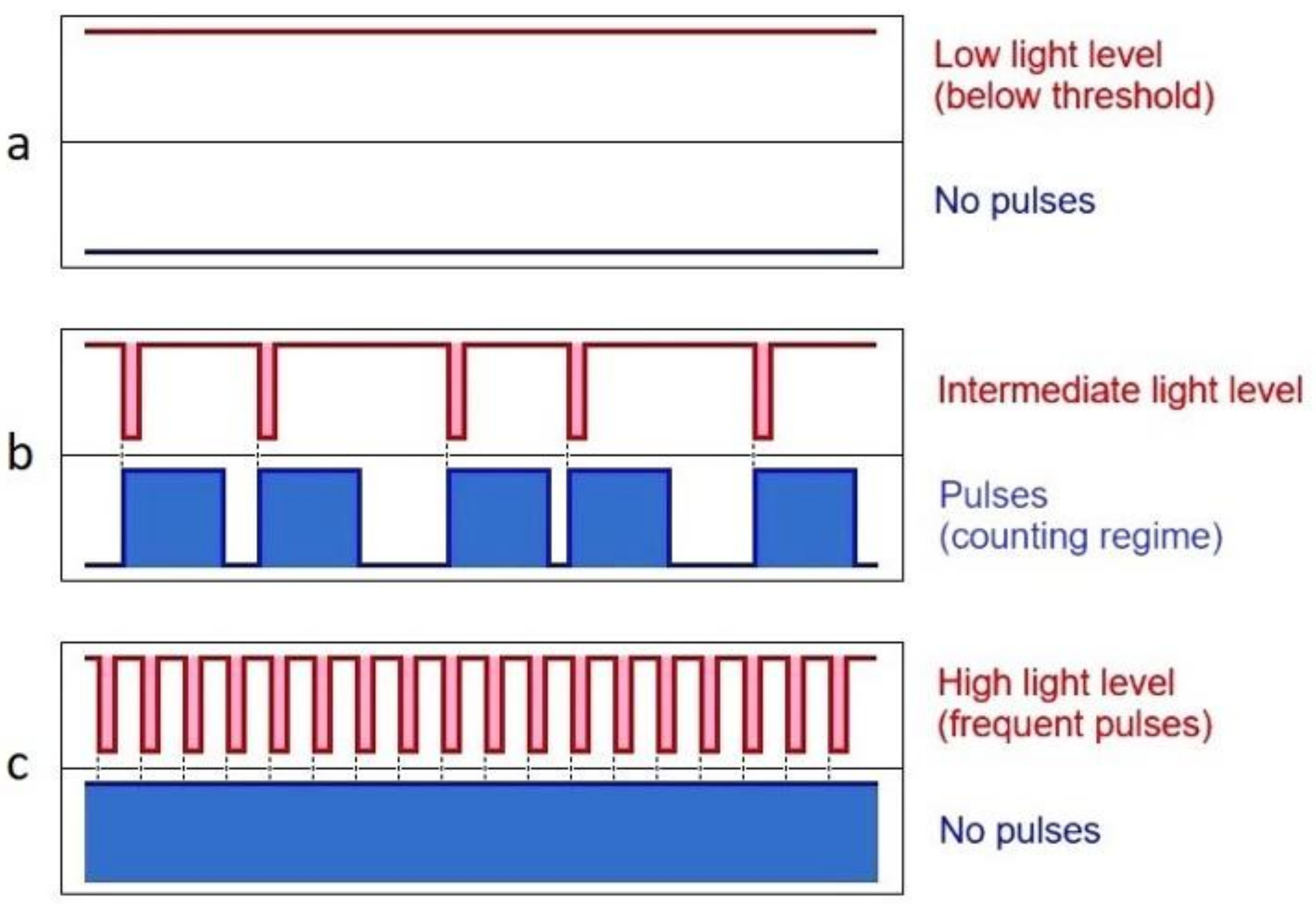


Structure of human hand in cross-section

Very difficult to work with such an object with complex structure and variable thickness. The non-uniformly scattering and absorbing elements distributed unevenly by the area and thickness.

Scanning of non-uniform bulk objects

Procedure #1: TSOP output signal inverting & stretching



OUTCOME:

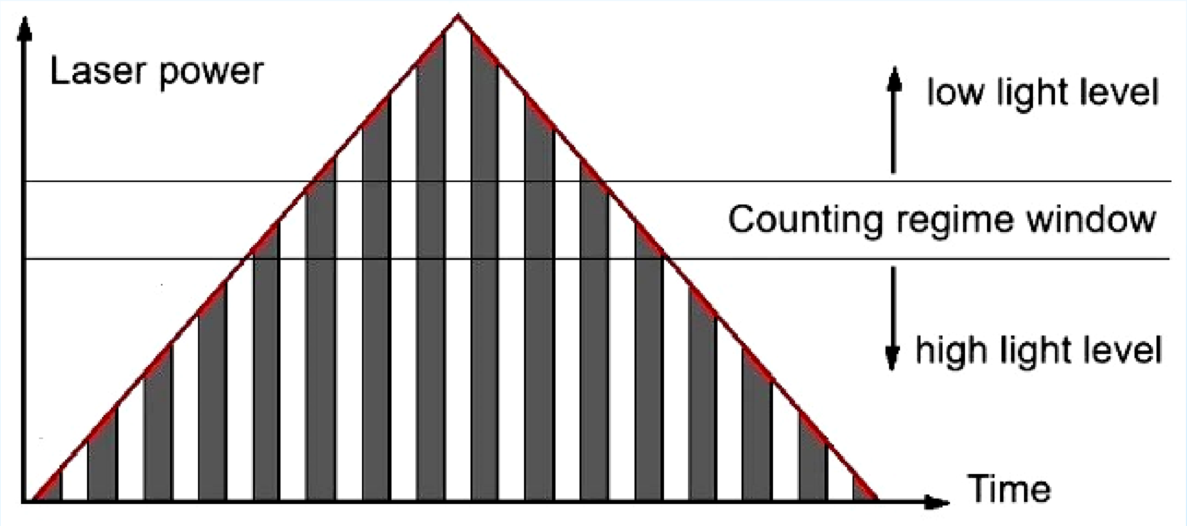
The signal reveals only in relatively narrow intensity range (“counting window”).

Both weak light (below detection threshold) and strong light (saturation) give a ZERO signal.

Scanning of non-uniform bulk objects

Procedure #2: Triangular envelope modulation of laser radiation

Such modulation (linear variation of laser power) is applied in order to swipe the “counting window” during the measurement, thus adjusting illumination level to the optimal detection conditions.



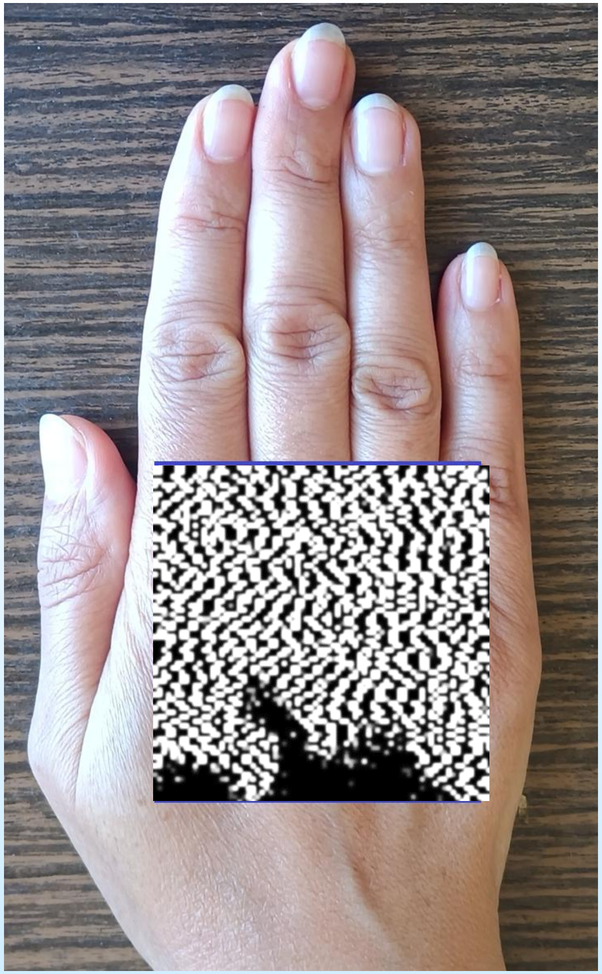
Effectively, it works as an automatic gain control.

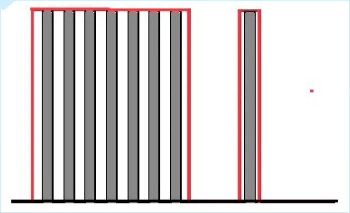
OUTCOME:

Independently of the signal level (above the threshold), it will be recorded with nearly invariable magnitude.

The overall background variations are being lifted.

Scanning of non-uniform bulk objects





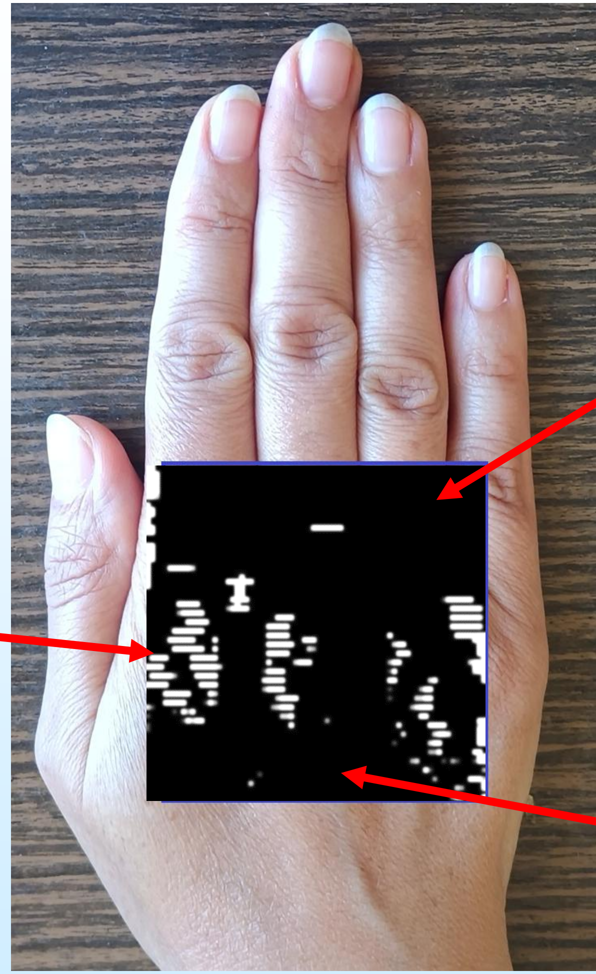
“Proportional” image obtained using NEC repeat code double modulation obviously fails.

Except the area where the transmitted light is below the detection threshold (lower black region), practically all the image is saturated (white).

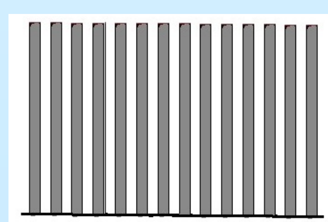
Scanning of non-uniform bulk objects

Strong light – no signal

Stretched pulse regime visualizes the image in relatively narrow intensity range

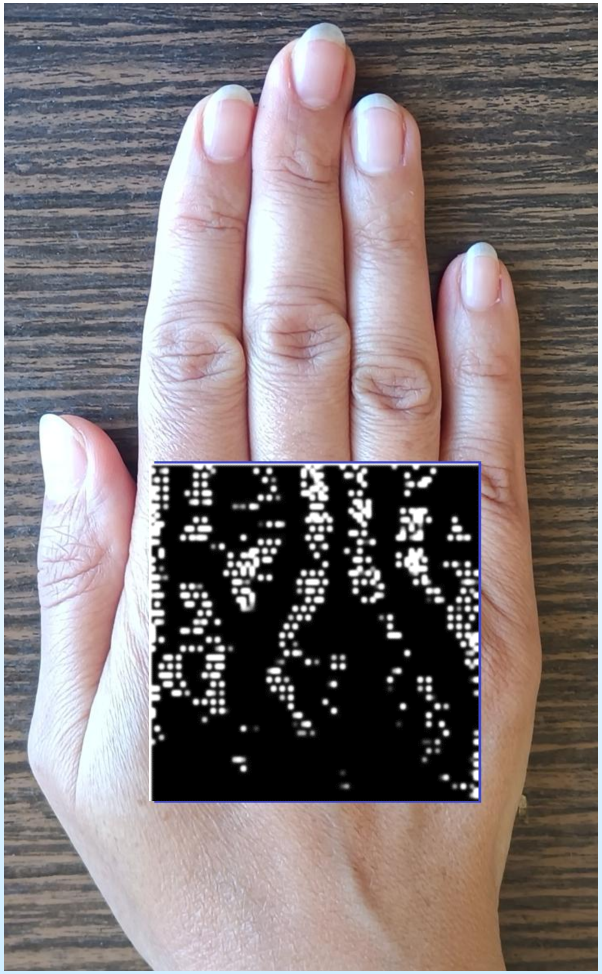


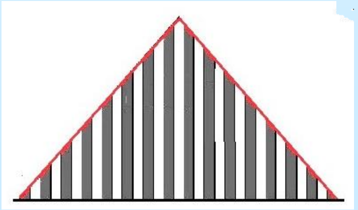
Weak light – no signal



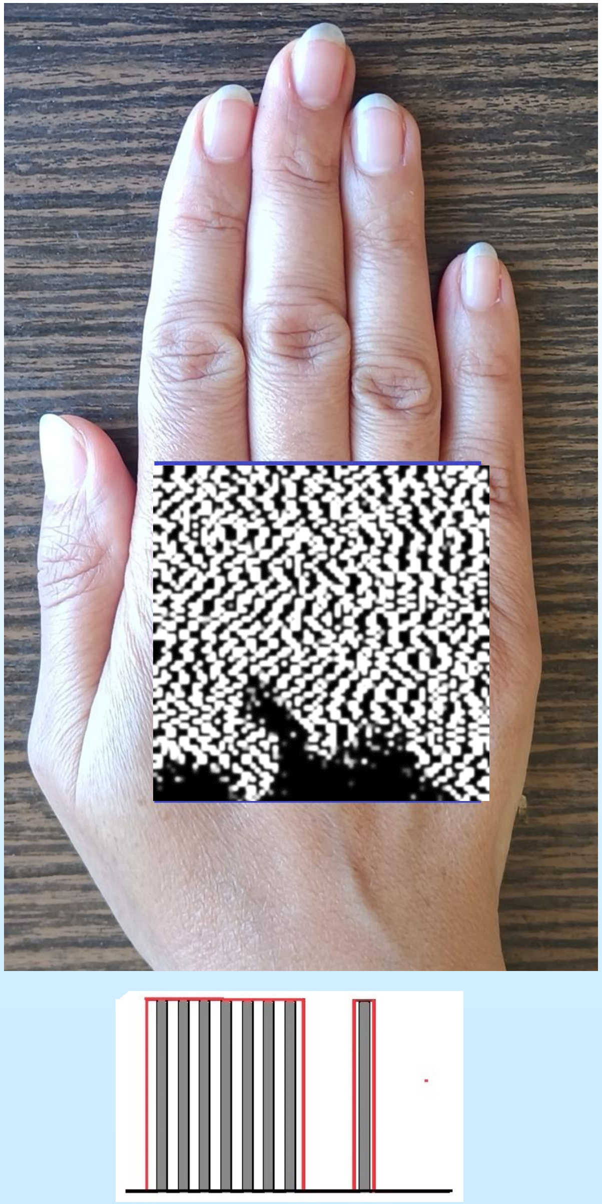
Scanning of non-uniform bulk objects

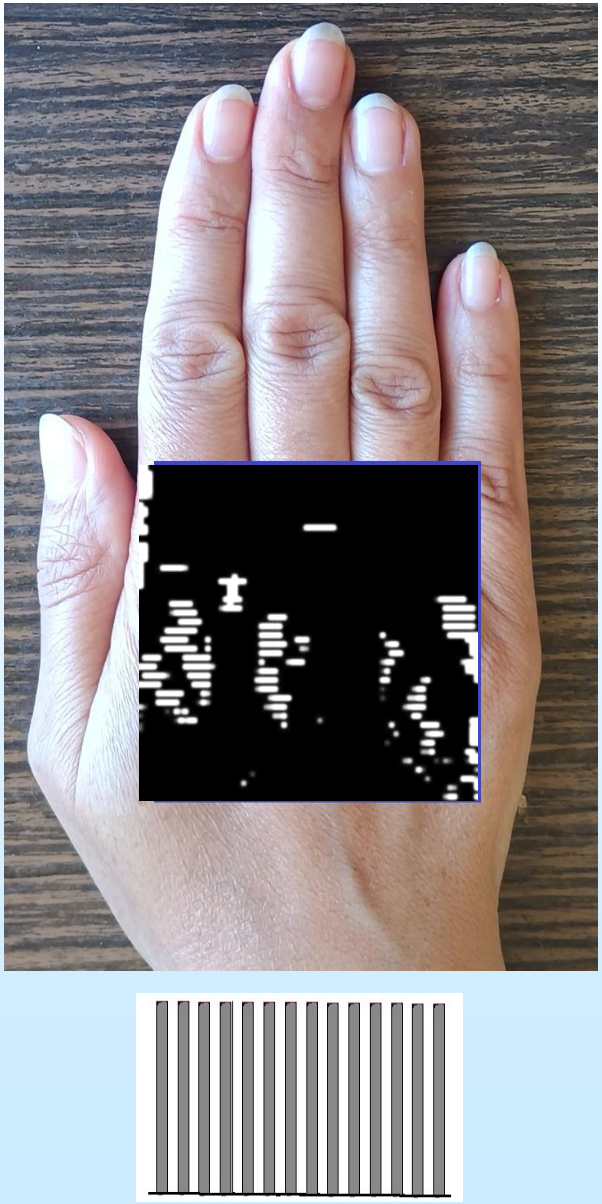
The image obtained using double triangular modulation reveals the structure (evenly, almost regardless of thickness).

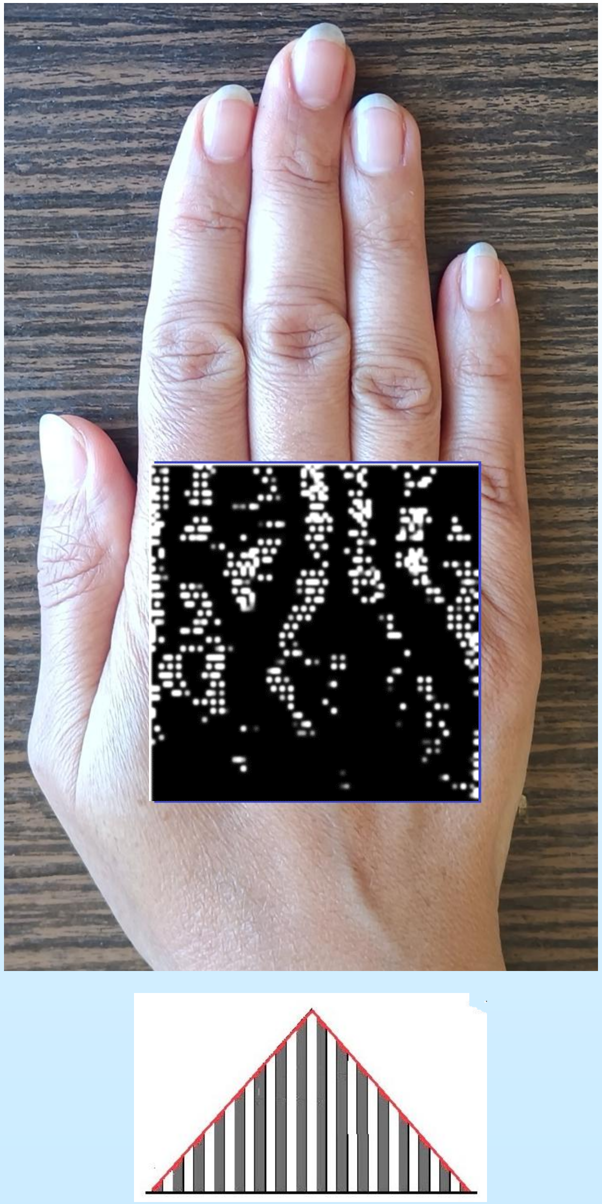




Scanning of non-uniform bulk objects



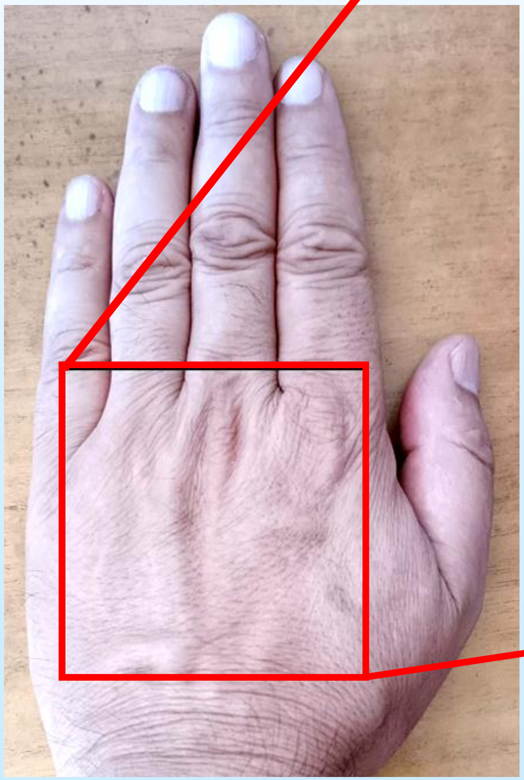




Scanning of non-uniform bulk objects

Image of human (mine ☺) palm recorded with double-modulated laser light (38 kHz rectangular "carrier" + 100 Hz triangular "envelope")

Scanning area:
60 x 60 mm
(1 px = 1 mm)



Number of levels of gray: 6

The picture does not change with repeated scans, unless you tighten the wrist with a tourniquet

Maximum thickness: 35 mm
Minimum thickness: 20 mm

Most likely, the observed structure predominantly corresponds to the vascular (arterial) system

Scanning of non-uniform bulk objects

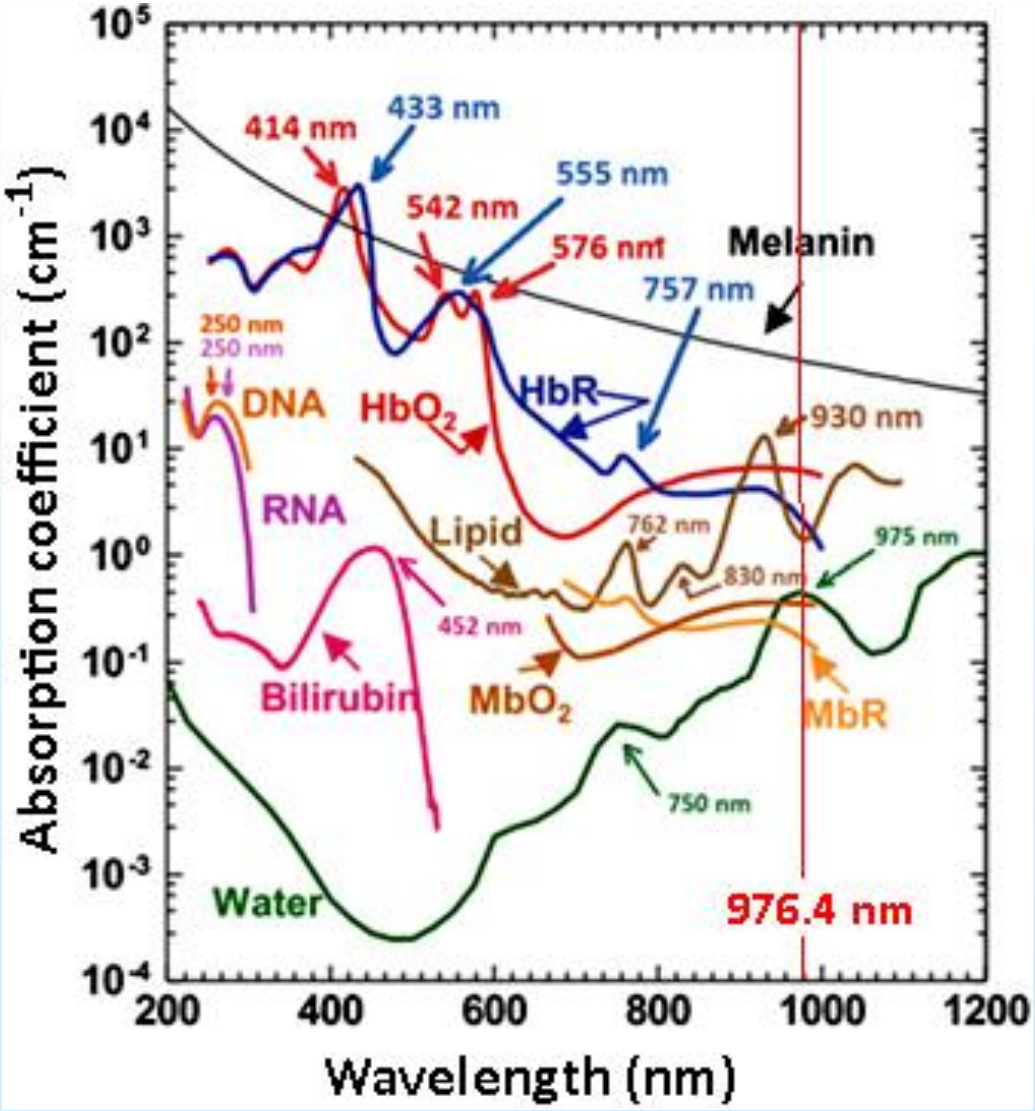
What is the recorded structure?

Muscle and other soft tissues, the skin cause a huge diffuse scattering.

Chromophores (hemoglobin, melanin, bilirubin, water, etc.) cause wavelength-dependent absorption.

Pronounced structure in the image can be expected from structured organs: bones, vascular system, tendons, etc.

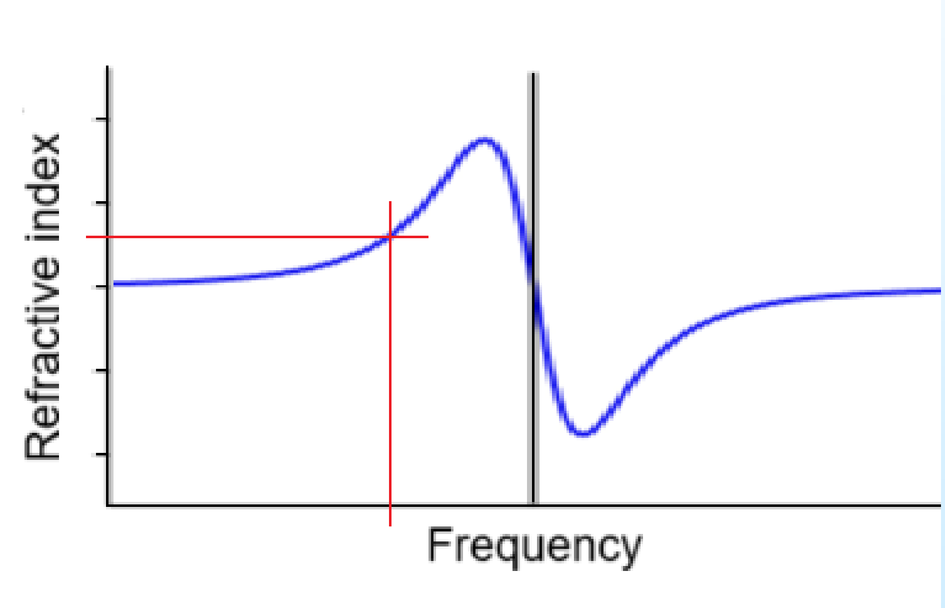
At λ = 976 nm, the bones absorption is low and close to the water absorption; the highest absorption has HbO2 (arterial blood).



Scanning of non-uniform bulk objects

Studies with “optical clearing” agents and dyes

Treatment of skin with optical clearing agents and solvents (dimethyl sulfoxide, propylene glycol, glycerol), as well as dye agents (tartrazine, ponceau 4R, indigo carmine)

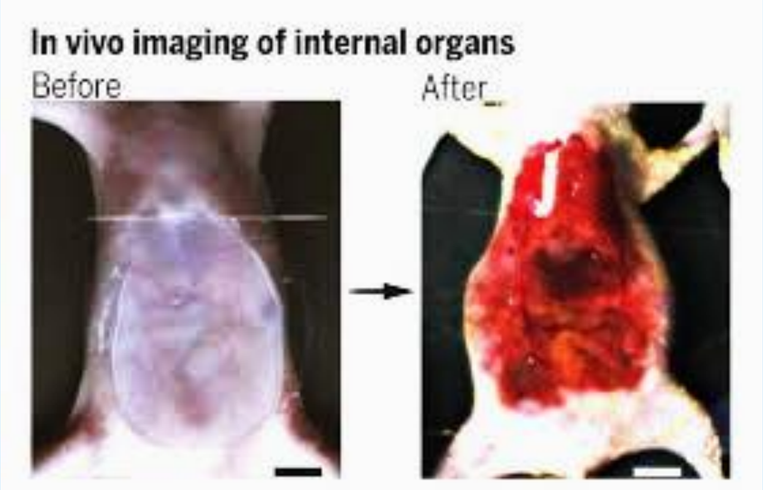


Z. Ou, Y.Sh. Duh, N.J. Rommelfanger *et al.*, “Achieving optical transparency in live animals with absorbing molecules”, **Science**, Vol. 385, Iss. 6713 (2024)

Expected outcome:
Enhanced resolution and sensitivity

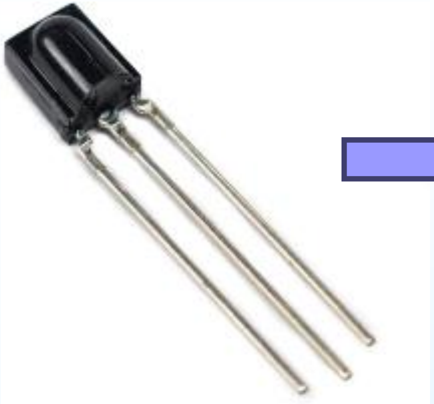
Real outcome:
Minor improvement

Reason:
Low efficiency when working with ballistic light



Performance optimization

Replacement of the VS1838 TSOP photoreceiver with a patented home-made short pulse photodetector



What is optimized:

- Detection wavelength: from 940-1000 nm to 450-1650 nm
- Increased possible scanning speed: 20 times
- Decreased needed illumination average power: up to 25 times (below the maximum permissible level of 200 mW/cm^2)
- Possibility of operation at any carrier modulation frequency

Sensitive selective detection of > 10 ns light pulses with > 20 pJ energy, immune against up to 20000 lux back-ground illumination

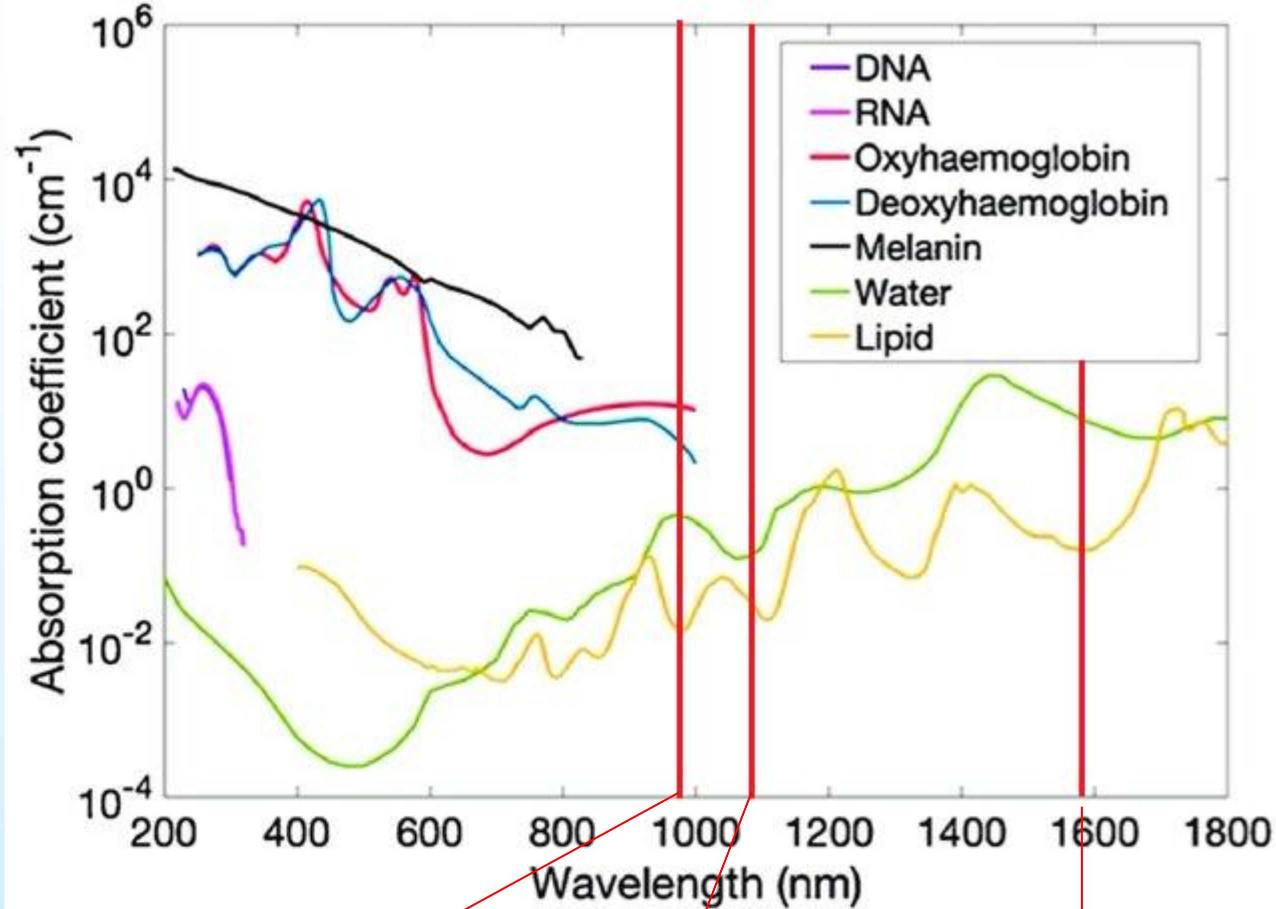
A. Papoyan, "Pulsed optical signal receiver", RA patent 720Y / G01J, Industrial Property, N3/2, page 7, 2022

Performance optimization

Exploring lasers with different wavelengths

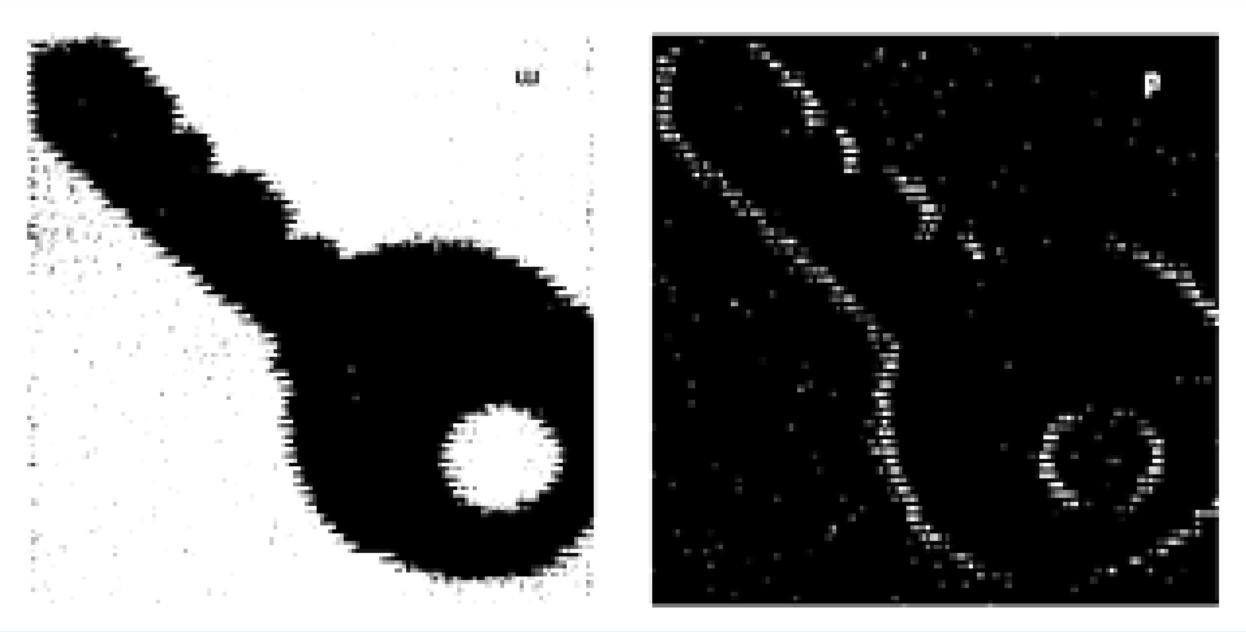
Pigtailed butterfly diode laser

Choosing appropriate wavelength for different biological chromophores and structures



λ = 976 nm **λ = 1075 nm** **λ = 1590 nm**

Scanning of planar scattering objects



$f_{mod} = 1$ kHz $f_{mod} = 100$ kHz

Model object: printed key symbol hidden in the stack of white paper. Laser: λ = 1075 nm

New photoreceiver:

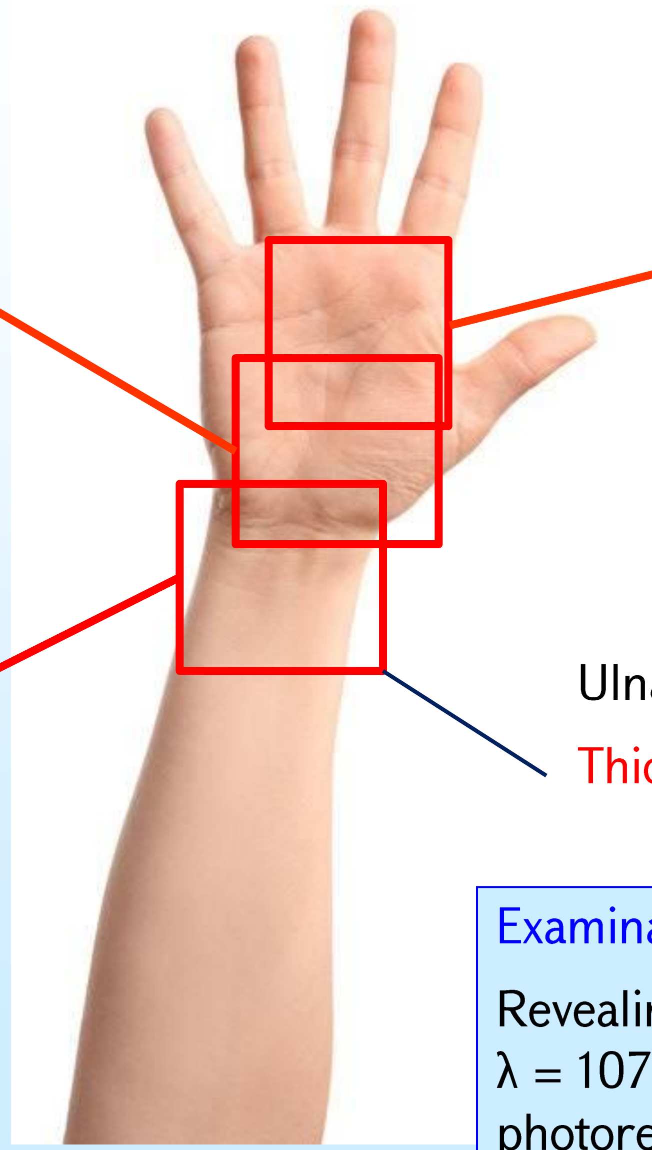
Easy switching from "proportional" (left) to "contour" (right) imaging regime.

The only parameter to change is modulation frequency (duty cycle with 9 μs rectangular pulses)

Spatial resolution for flat model objects is 1 pixel (down to 0.2 mm)

Scanning of non-uniform bulk objects

proportional



contour

Ulna and Radius bones:

Thickness up to 50 mm!

Examination of biological objects:

Revealing the bone structure with λ = 1075 nm laser radiation (new photoreceiver)

Scanning of non-uniform bulk objects

Essential water absorption makes λ = 1590 nm wavelength inappropriate for *in vivo* imaging of biological objects

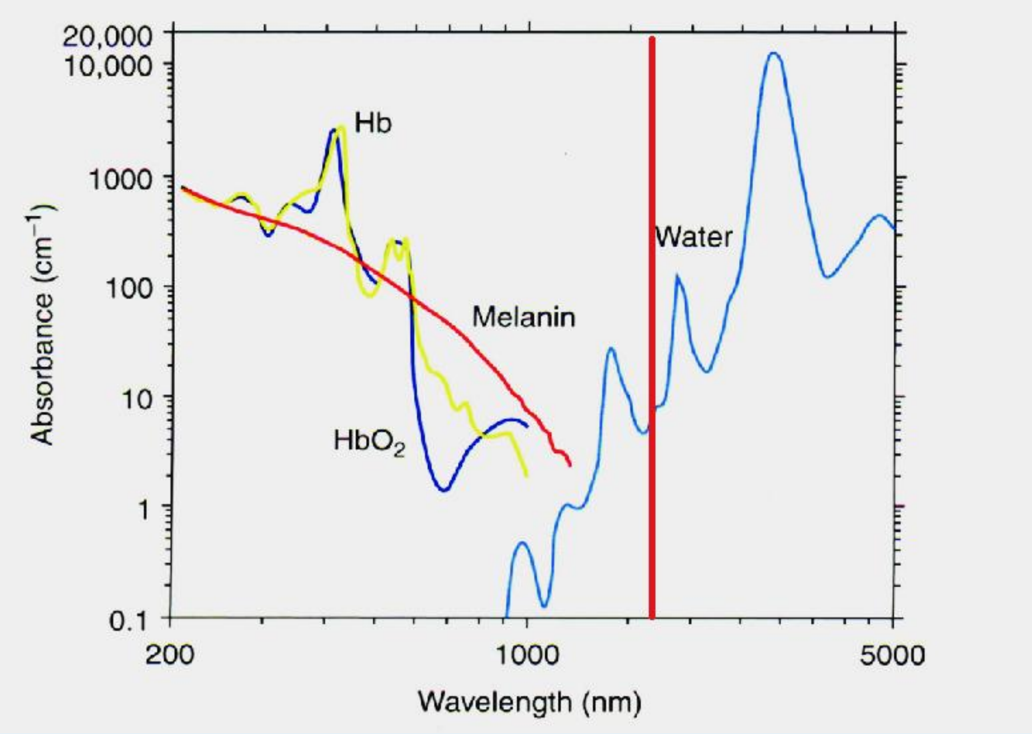


Image of dried lizard recorded with λ = 1590 nm laser radiation. One can see the spin, stomach area and the developing egg.

The outlook

The follow-up studies will be aimed at:

- The use of other, more universal pulsed photodetectors, developed and patented at the Institute for Physical Research, operating in the laser radiation modulation mode with subsequent lock-in detection of signal.

  The expected result is an expanded range of wavelengths, a reduction in scanning time, and an increase in scanning speed.

- Optimization of ballistic photon detection by implementing a telescopic system for the narrow-waist illumination and efficient light collection.

  The expected result is an improvement of spatial resolution of imaging, possibly also recording of tomographic images.

- *In vivo* biomedical studies (possibly combined with AI enhancements).

  The expected result is a visualization of bone, vascular and tendon structure of up to 50 mm-thick organs for revealing of tumors and other pathologies.

- Optical clearing of the skin using safe chemical agents.

  The expected result is an enhancement of transmitted light and improved spatial resolution.

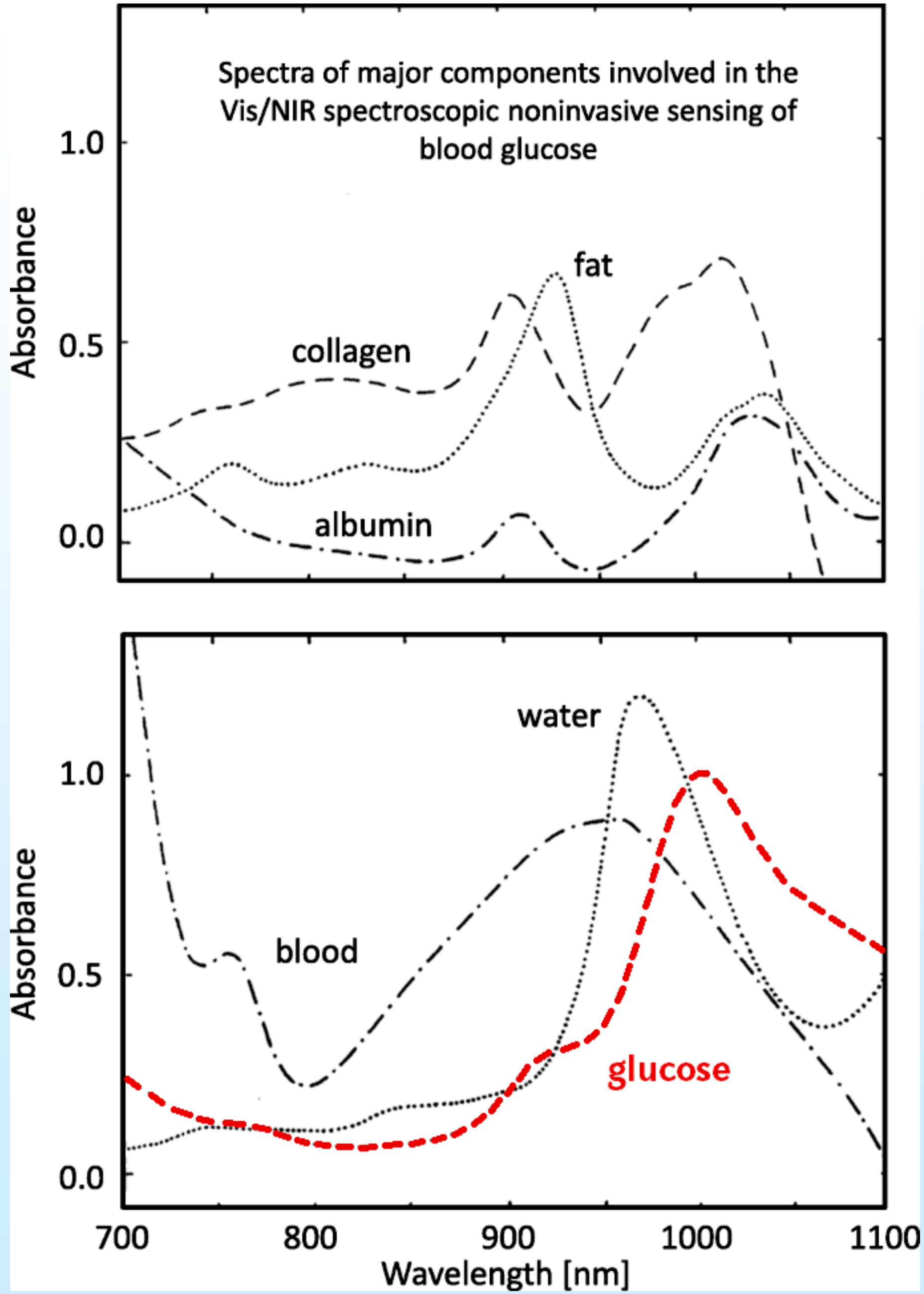
Project sub-tasks

II stage (2 years)

Development of an optical non-invasive glucometer

Optical glucometer

Absorption spectra of glucose and other chromophores in human blood →



Most of non-invasive optical glucometers explore absorption at a certain wavelength.

Low precision:

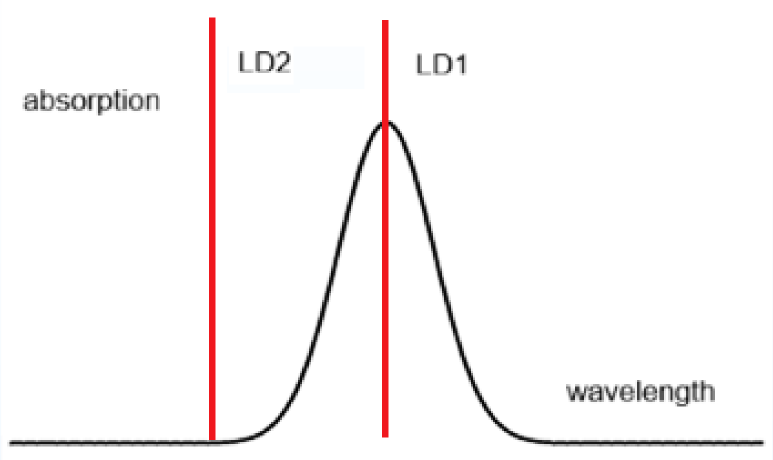
- sample thickness uncertainty, scattered light
- overlapping contribution from other chromophores

Our goal:

- higher selectivity
- higher precision

of measurement

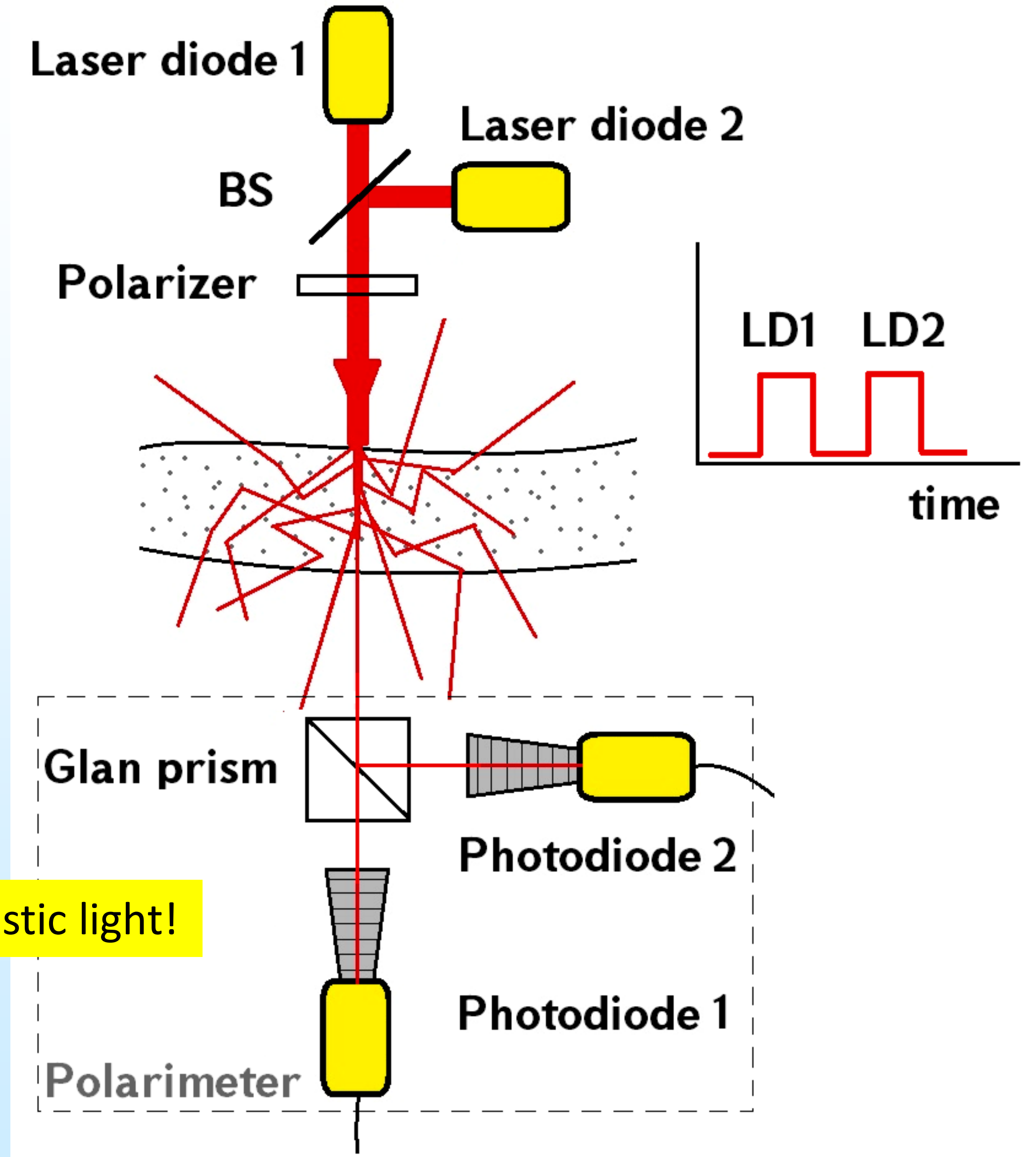
Optical glucometer



Combined double-wavelength absorption-polarization principle

LD1	LD2
840 nm	800 nm
930 nm	900 nm
1020 nm	970 nm
↑	↑
absorption	rotation of polarization plane

ballistic light!



Schematic diagram of the laboratory prototype:

Optical glucometer

Studies are under way,

To be reported at Annual Fall Meeting 2026

International collaboration, new projects

Joint research work and new project discussions with the project collaborator Prof. Valery Tuchin (visiting Armenia 8-15 Nov. 2025)

Discussions on joint Horizon-Europe project with Prof. Riccardo Cicchi (Istituto Nazionale di Ottica, CNR-INO, Firenze, Italy) and colleagues during their visit to Armenia

Contributors

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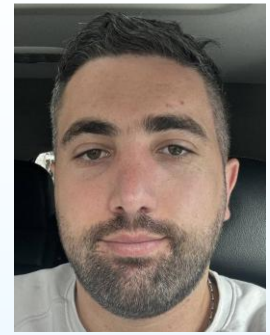

Pavel Saakyan

Hrachya Sultanyan

Valery Tuchin

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Diploma work 2024-2025: Felix Sargsyan (Quanta Master program)

Published articles

Scientific:

1. A. Khanbekyan, S. Shmavonyan, P. Saakyan, H. Sultanyan, M. Movsisyan, A. Papoyan, “A simple optical scanner for transmission imaging of biological objects”, **Optics and Spectroscopy**, v.132, No.9, pp.932-936 (2024). Q4
2. S. Shmavonyan, A. Khanbekyan, M. Movsisyan, A. Papoyan, “Scanning technique for direct optical transmission imaging of highly-scattering objects”, **Optics and Lasers in Engineering**, v.184, 108633 (6p.) (2025). **Q1**
3. S.V. Shmavonyan, A.M. Khanbekyan, F.A. Sargsyan, M.E. Movsisyan, A.V. Papoyan, “Method of pulsed optical imaging of strongly scattering objects”, **Journal of Contemporary Physics (Armenian Academy of Sciences)**, v.60, No.3 (2025). Q4

Popular:

Ա. Պապոյան, «Կենսաբանական օբյեկտների օպտիկական պատկերագրում», **Գիտության աշխարհում**, 2024, N4, էջ 26-31.


Thank you for your attention!