



uTIRF Biodetection Station and iDiagnostics Application Development Kit

iDiagnostics - the Handheld Future of Medicine
accurate, rapid, personalized, and affordable molecular diagnosing

Develop accurate and rapid molecular diagnostic tests based on panels of protein, nucleic acid, and metabolite biomarkers. Use uTIRF biodetection station and iDiagnostics Application Development Kit

The early detection of cancer, cardiovascular and other diseases, preventing pandemics, and other healthcare tasks require a highly sensitive, accurate, rapid, and yet affordable molecular diagnostics. Eleven years of research at TIRF Labs have resulted in the development of such a technology: a handheld platform, named iDiagnostics. It is a thousand times more accurate than traditional methods, is rapid and robust, and yet is inexpensive.

The goal of TIRF Labs is to provide iDiagnostics to every family on the globe. This goal cannot be achieved by a single company; we envision a collective global effort from the diagnostics community using the Open Innovation Business Model, which will stimulate a flux of intellectual property (IP) in and out of the iDiagnostics project. TIRF Labs will be delighted to license the IP of other groups and will offer the opportunity to license our own IP, in certain cases free of charge.

To facilitate all of the stages of this challenging project, from biomarker discovery, to clinical testing, TIRF Labs offers the uTIRF biodetection station and the Application Development Kit (ADK). Figs. 1 and 2 show the optical scheme and photos of uTIRF, the lightguide-based TIRF accessory, and manual microarrayer. Fig. 3 shows the iDiagnostics handheld cradle, and reusable cartridges designed for the development stage. These products are available to all members of the diagnostic community, including academic, industrial, and government research groups. The NIH, FDA and CDC will be involved in the coordination of the collective efforts. Two main products create the foundation for the collective project: (i) uTIRF - a multifunctional biodetection station, which is sensitive down to single molecules and includes lightguide-, prism-, and objective-based TIRF, a low light CMOS camera, three-color illuminator, and 1X, 4X, and 60X objectives, as well as (ii) the iDiagnostics ADK, which consists of the TIRF handheld cradle, cartridge blanks, manual microarrayer, and reagents kit. TIRF Labs has already received numerous requests from research groups worldwide to supply these products. In the middle of 2018 we plan to start supplying these products along with experimental protocols. Several groups have already joined our project. We have incorporated their feedback and will incorporate future comments from our future customers in the next releases of the uTIRF and ADKs. We will supply advanced hardware, software, reagents, development tools, protocols, videos, and other support to accommodate the requirements for different diagnostic applications.

The arrays of bioassays printed at the surface of iDiagnostics slides include assays for detecting protein, nucleic acid, metabolite biomarkers. The arrays contain internal controls to ensure reliability and calibration. The cartridge is equipped with a 20-microliters flow cell, which encompasses the microarray. iDiagnostics requires no or minimum sample preparation. Whole blood can be analyzed after the addition of an anticoagulant. Simple sample preparation module is included in the cartridge; space is reserved for more complex sample preparation modules as will be required for applications developed in the future. For more information see iDiagnostics brochure, visit i-diagnostics.net website, and contact us via email: info@tirf-labs.com

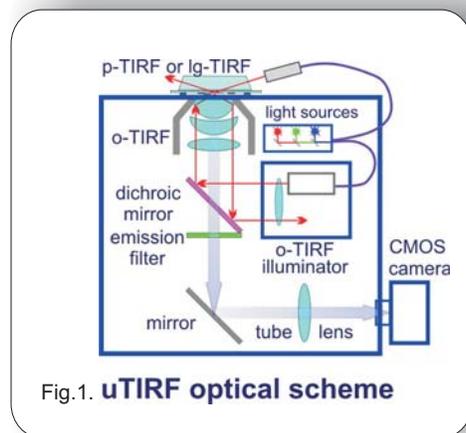


Fig.1. uTIRF optical scheme



Fig. 2. uTIRF with pTIRF installed, IgTIRF - upper right, and manual microarrayer.



Fig.3. iDiagnostics handheld cradle with cartridges.

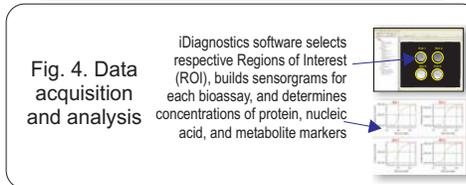


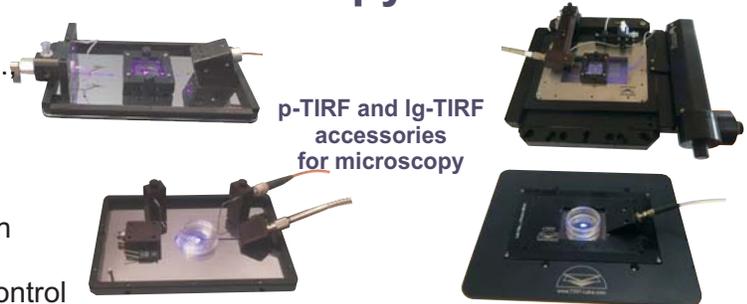
Fig. 4. Data acquisition and analysis

iDiagnostics software selects respective Regions of Interest (ROI), builds sensorgrams for each bioassay, and determines concentrations of protein, nucleic acid, and metabolite markers



Prism- and Lightguide-based TIRF Microscopy Accessories

- Single molecule detection
- Super-resolution microscopy: STED, PALM, STORM, ...
- Minimal stray light, crisp, high-contrast TIRF images
- Work with dry, water-, and oil-immersion objectives
- Use UV or visible excitation light 190-900 nm
- Use Petri-dish, open perfusion, or closed flow chamber
- Nested design - fits inside 96-well plate, K-frame, 4-inch round, or manual XY stages
- Optional temperature, dielectrophoresis, electric field control



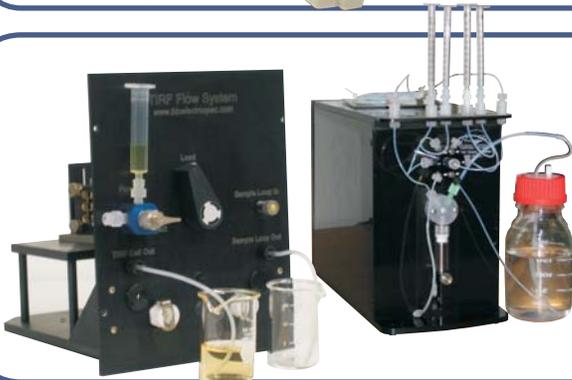
p-TIRF and Ig-TIRF accessories for microscopy

Turnkey Single Molecule Detection TIRF Microscopy Station



- Modular TIRFM stations include:**
- Fluorescence microscope
 - Ig-, p-, or/and o-TIRF microscopy flow systems
 - Low light EM CCD or sCMOS camera
 - Multi-color computer-controlled illuminator
 - Digital fluidics SmartFlow
 - Optional temperature and electric field control
 - Software for instrument control and data analysis

TIRF Accessories for Fluorometers



- **TIRF Accessory TA-1004** transforms a spectrofluorometer into a super-sensitive TIRF biosensor instrument
- Optional electrochemical, DEP and temperature control
- **SmartFlow** Fluidic System allows to run unattended TIRF experiments, measure sensograms to derive k_{on} and k_{off}
- Microfluidic system allows for handling nanoliter volumes

Single ion Channel Single Molecule Detection

fluorescence excitation

patch clamp pipette as light-guide

cell membrane

ion channel

pipette tip transmittance and excitation

pipette tip excitation only

1 micron

SC-SMD on microscope stage

Patch clamp technique combined with fluorescence single molecule detection

iDiagnostics

cellphone based molecular diagnostics

Real-time TIRF microarrays:
 Parallel supersensitive detection of protein, nucleic acid, and metabolite biomarkers



We extended TIRF into the 3rd dimension and invented iDiagnostics
Now you can hold a hospital laboratory in the palm of your hand