Epic BT® system integration, a compact and fully automated HTS label free platform

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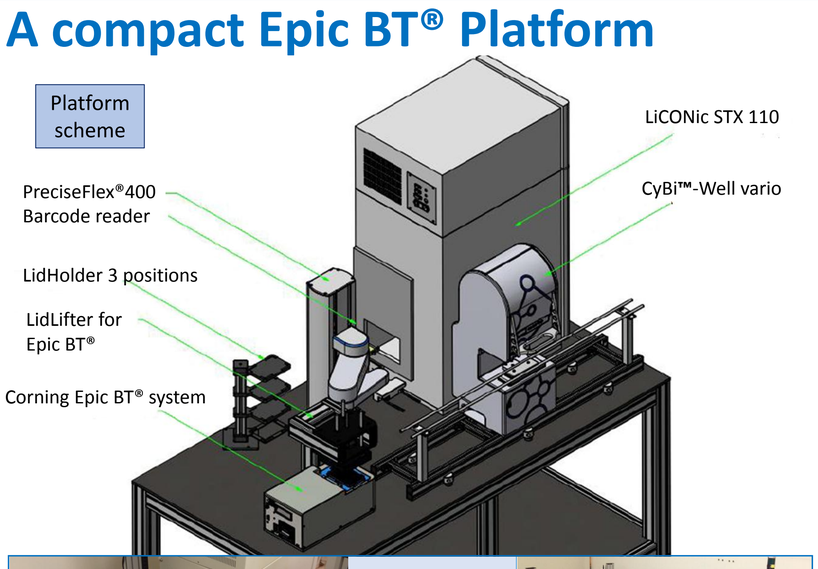
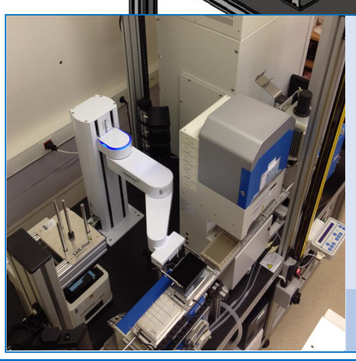
Label free approaches are now integral parts of the **High-Troughput Screening** toolbox. Without the use of any labeled compounds or proteins, this innovative technology is able to provide critical information about multiple biological activities including transduction pathways and molecular binding. Label free technologies have proven to be particularly useful for **GPCR deorphanization**.

To fully take advantage of its compactness and fast data acquisition (CCD camera) we choose to integrate the new Corning label free EPIC BT® optical **biosensor** system in an automated platform. This integration, never performed before for this reader, was conducted in collaboration with **HI-RIS Lab**, **Lab Services**, and **Corning**.

A compact Epic BT® Platform

Platform scheme

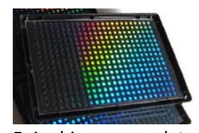




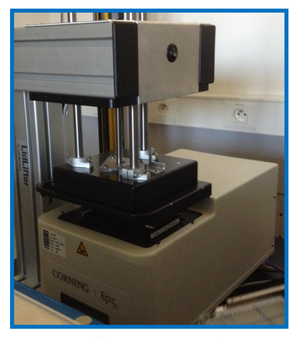
LidHolder

Platform photos

- Platform : 2m lenght * 1m depth
- up to 50 384/wells plates per run
- PreciseFlex®400 **safe moving gripper** ⇒ small footprint ⇒ quite silent and fast
- LiCONiC® STX 110 ⇒ **automated incubator** ⇒ CO2 and °C controlled ⇒ for **110 plates.**
- **CyBi™-Well Vario** five positions pipetor with 50 plates stackers and a washstation
- Epic BT® reader ⇒ CCD camera ⇒ **3 sec. data acquistion** (384 Corning plate)
- **Barcode reader** : Each cells and compounds plates are identified ⇒ enable the process following and the reading data generation
- a 3 positions **LidHolder**
- Intermediate plate pod position ⇒ landscape or portrait plate handling
- A **temperature controlled environment :** from the LiCONiC® incubator to the CyBi™-Well thermocontrolled conveyor and the Epic BT® temperature controlled Lidlifter
- BatchFile : LabServices software upgrade for barcoding data generation

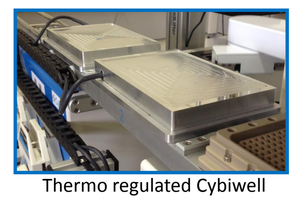


Epics biosensors plates



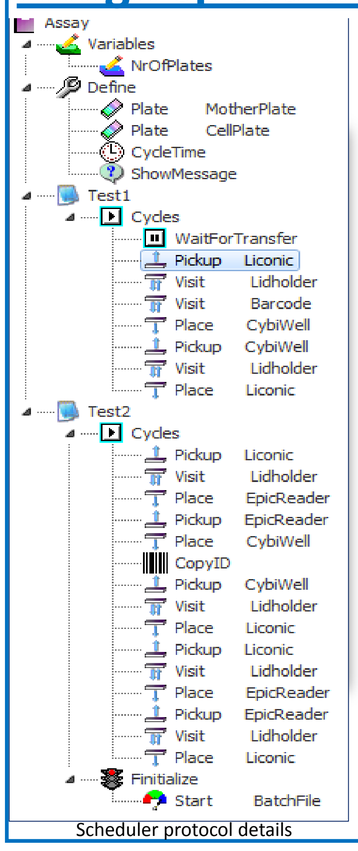
Thermo regulated and automated Epic BT lid

The standard Epic BT® is not an H.T.S. reader. It has no automated plate loading position. **HI-RIS Lab** and **Lab Services automated** the reader, developed a specific **driver** and manufactured a **new inlay** for a better plate positioning on the reader lens.



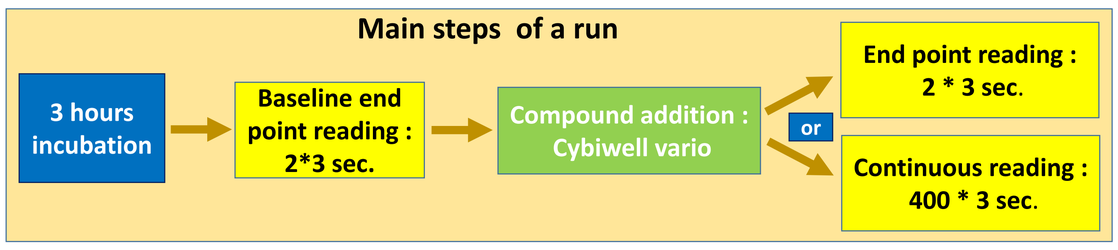
Thermo regulated Cybiwell conveyor

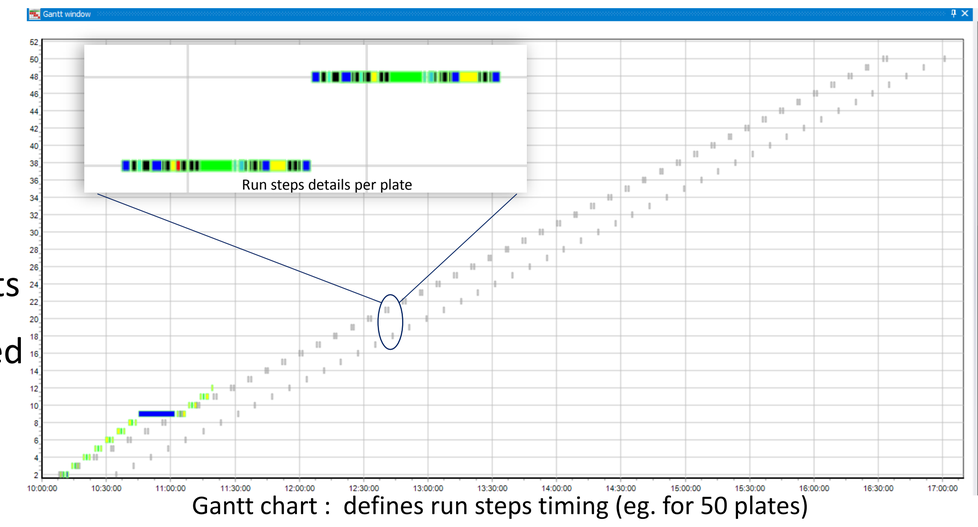
A high speed data acquisition and a fast communication robotics



Scheduler protocol details

- **Multi-task** scheduling : optimizes plates handling (cf. script details on the left scheme)
- The **Gantt chart** ⇒ gives the timing of each process steps before a run
- The Epic BT® **CCD camera** ⇒ data generated in 3 secondes ⇒ perfect for **kinetics readings**



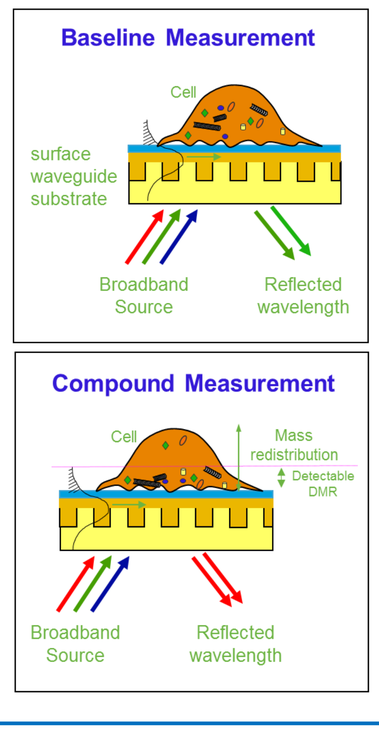


Gantt chart : defines run steps timing (eg. for 50 plates)

- **High-speed communication** between the server and the apparatus clients
- The main application control the **server** and each apparatus are controlled by a **client**.
- We, via the clients, control each apparatus and watch their **status** during the run on the scheduler dashboard.
- The communication configuration by I.P. addresses is compatible with the **stand-alone use** of each platform components

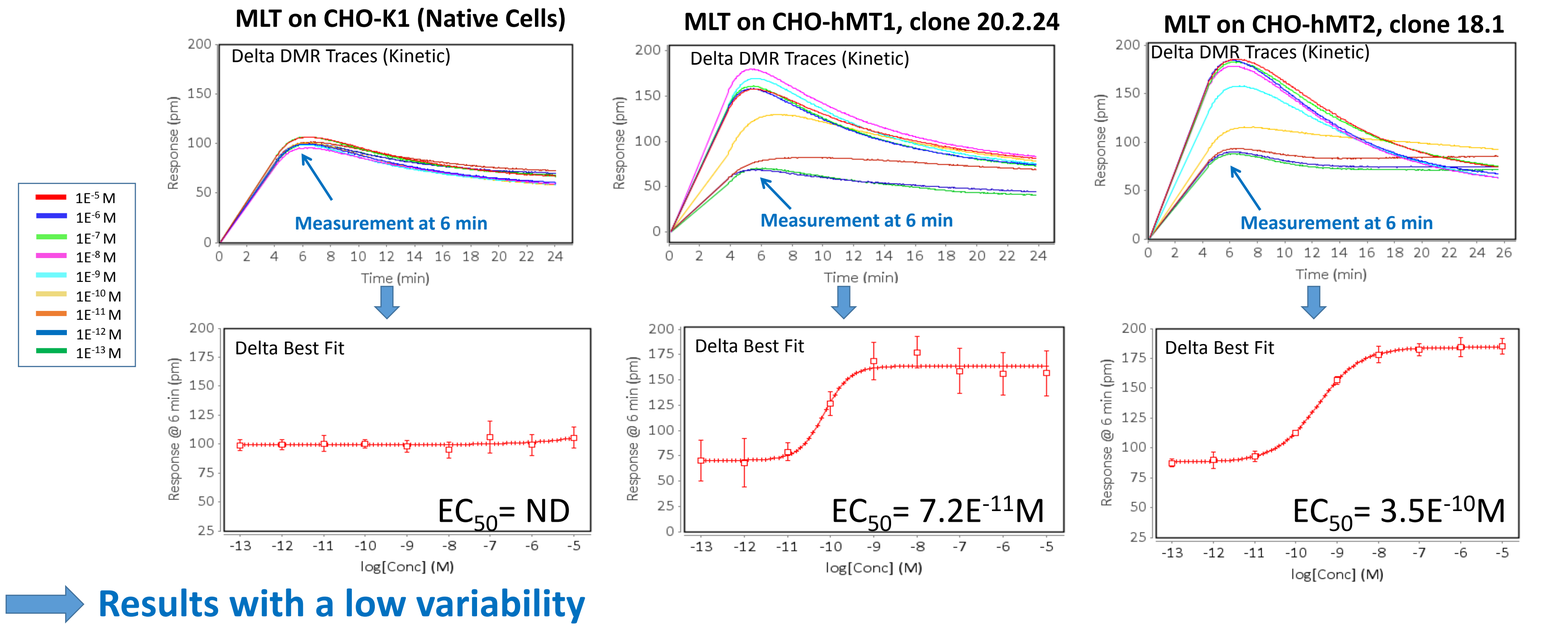
Epic® assays use optical biosensors to measure very small changes in index of refraction (related to mass)

It measures changes of local index of refraction resulting from the ligand-induced Dynamic Mass Redistribution (DMR) within the bottom region (~150nm) of the cell monolayer. Change in index results in the shift of the reflected wavelength.



Melatonine (MLT) profiles in hMT_1, hMT_2 and native CHO cell lines

- ✓ Seeded culture plates, fibronectin coated, with 10000 c/w (overnight incubation at 37°C, 5% CO_2)
- ✓ Cells equilibrate for 3 hours in HBSS Buffer + Hepes 20mM + BSA 0.05%
- ✓ 10µl compounds addition
- ✓ Continuous (every 3 sec.) data acquisition for 25 min with controlled temperature platform at 28°C



Results with a low variability
Assay window is satisfactory
Calculated EC_{50} are similar to already measured ones (Binding & Dielectric impedance)

Conclusion:

The Epic BT® platform is a very powerful and flexible tool, functional for our screening activity including the analysis of transduction pathways, GPCR deorphanization, biochemical bindings tests and enzymatic assays.