Asymmetric-detection Time-stretch Optical Microscopy (ATOM) - An ultrafast optical imaging technology for biomedical diagnosis

最新高速光學顯微成像技術及其醫學診斷應用

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新聞發布會 Press Conference
日期：2014年2月20日
時間：下午3時至4時

香港大學
The University of Hong Kong

現時光學成像系統
Current optical imaging systems

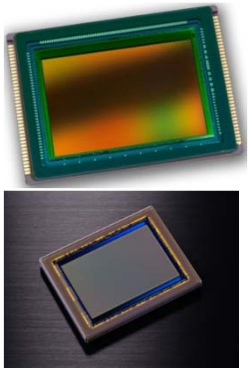
數碼相機 (Digital cameras)

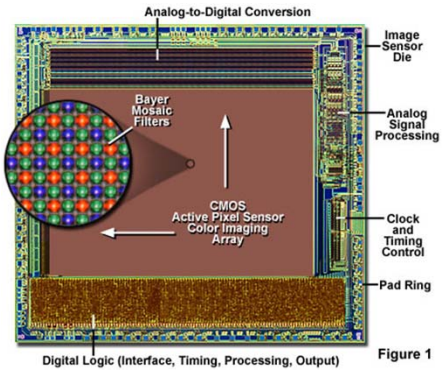
網路視像相機(Webcams)

智能手機
(Smartphone cameras)

光學顯微鏡(Optical microscopes)

核心技術: CCD and CMOS 影像感應器
Core technologies: CCD and CMOS image sensors





普通質素(Consumer-grade):
- 成像速度(frame rate):每秒**1-10's** 幀 (1-10's Hz)
- 曝光時間 (exposure time): **1-100** 毫秒 (1-100 ms)

高端質素 (Advanced-grade):
- 成像速度(frame rate):每秒**1000's** 幀 (1000's Hz)
- 曝光時間 (exposure time): **0.001** 毫秒 (0.001 ms)

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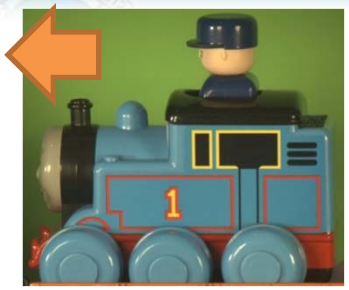
現時影像感應器之限制 – 速度與敏感度之間的取捨

Fundamental limitation in current image sensors – Speed vs sensitivity



快門 – 開
(Shutter opened)

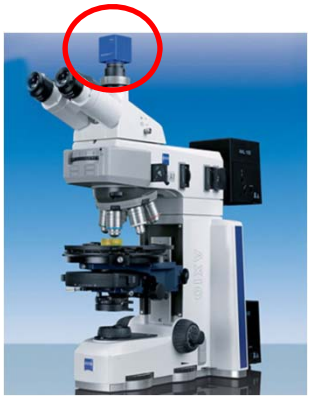
快門 – 關
(shutter closed)

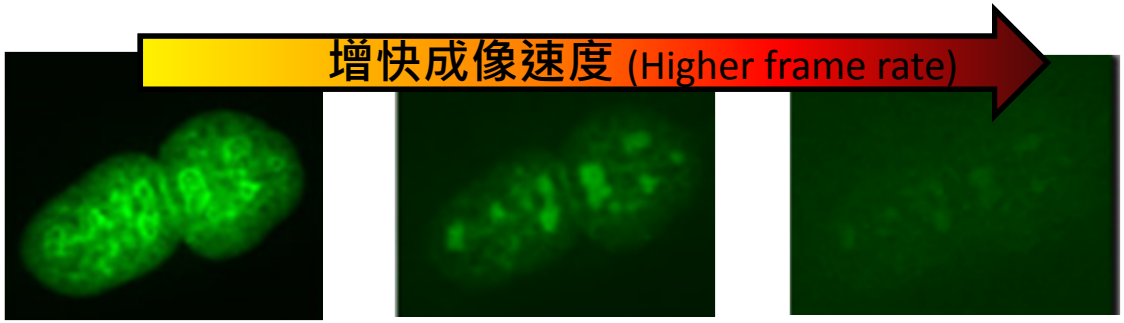
時間 (Time)

時間 (Time)

....同樣問題出現於生物顯微鏡拍攝

Also applied to biological cell imaging





每秒 0.1 幀
Frame rate : 0.1 Hz

每秒 1 幀
Frame rate : 1Hz

每秒 10 幀
Frame rate : 10Hz

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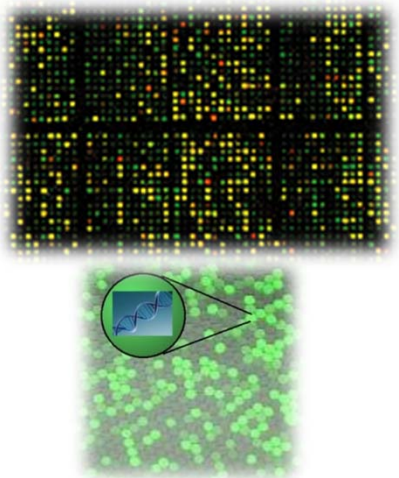
高速生物顯微鏡有利高效率醫學診斷

Needs for high-efficiency medical diagnosis

高效率醫學診斷

High throughput + High-content diagnostics

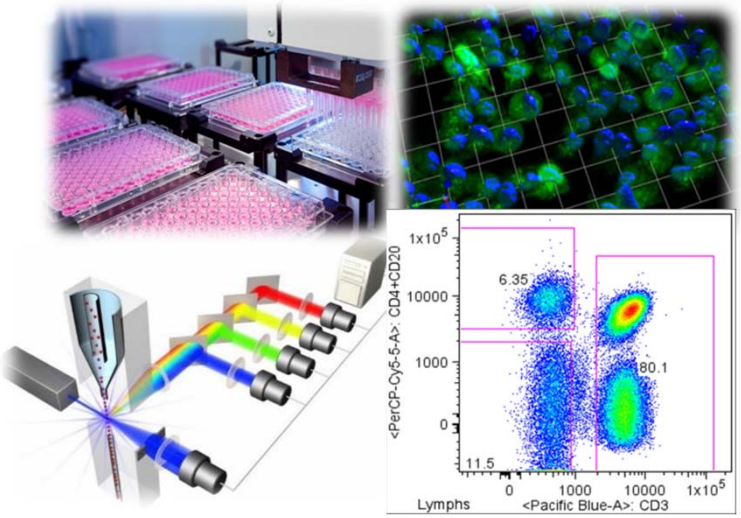
短時間內處理大量生物樣品的數據，有效辨識每一組織, 細胞, 甚至生物分子的特徵



生物分子化驗

例如:基因分析

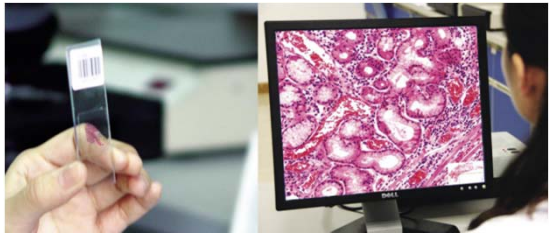
DNA microarray

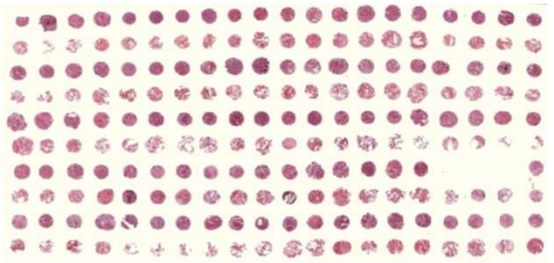


細胞化驗

例如: 流動細胞儀

flow cytometry



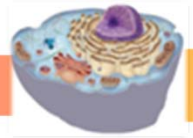


病理組織化驗

例如:全切片成像

Whole-slide imaging

生物分子(biomolecules)



細胞 (cells)

組織 (tissues)

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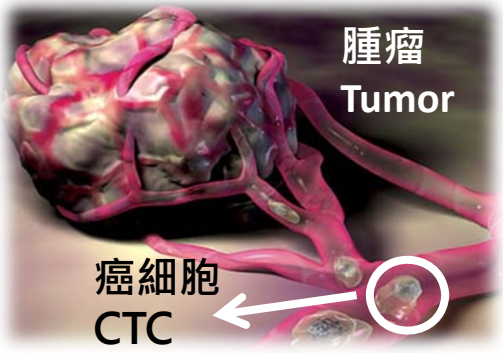
例子:偵測血液中微量癌細胞

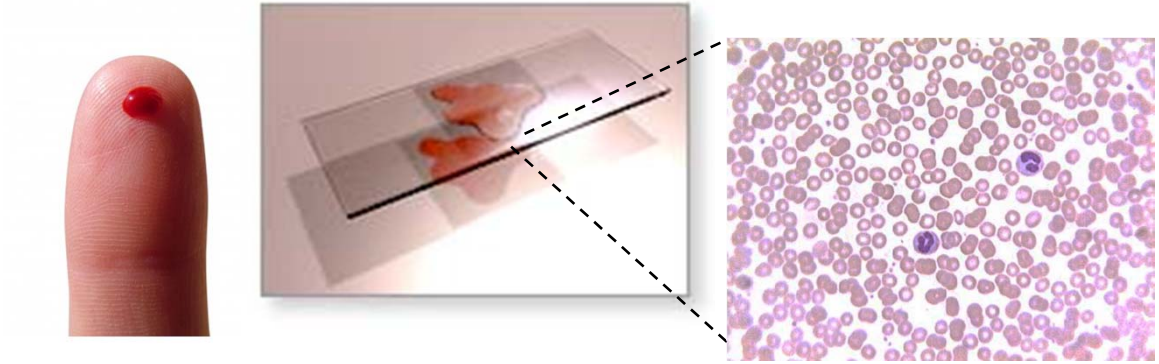
Example: Detecting rare cancer cells

- 早期癌症時, 血液中只含極微量癌細胞: (*Circulating tumor cells (CTCs)* are extremely rare)

→大約每一毫升血液中就有一個癌細胞 (~ 1 cell in milliliter of blood)

→但一毫升血液中, 有 數十億個血液細胞 (1 mL = few billions of blood cells)





- 利用現今高速影像感應器 (today's fastest cameras):
  - 可達不高於每秒拍攝 1000 個細胞之速度
    (<1000 cells per seconds is possible.)
  - 記錄所有血液細胞 → 需時2個月!!!
    (*2 months* to find a single cell)

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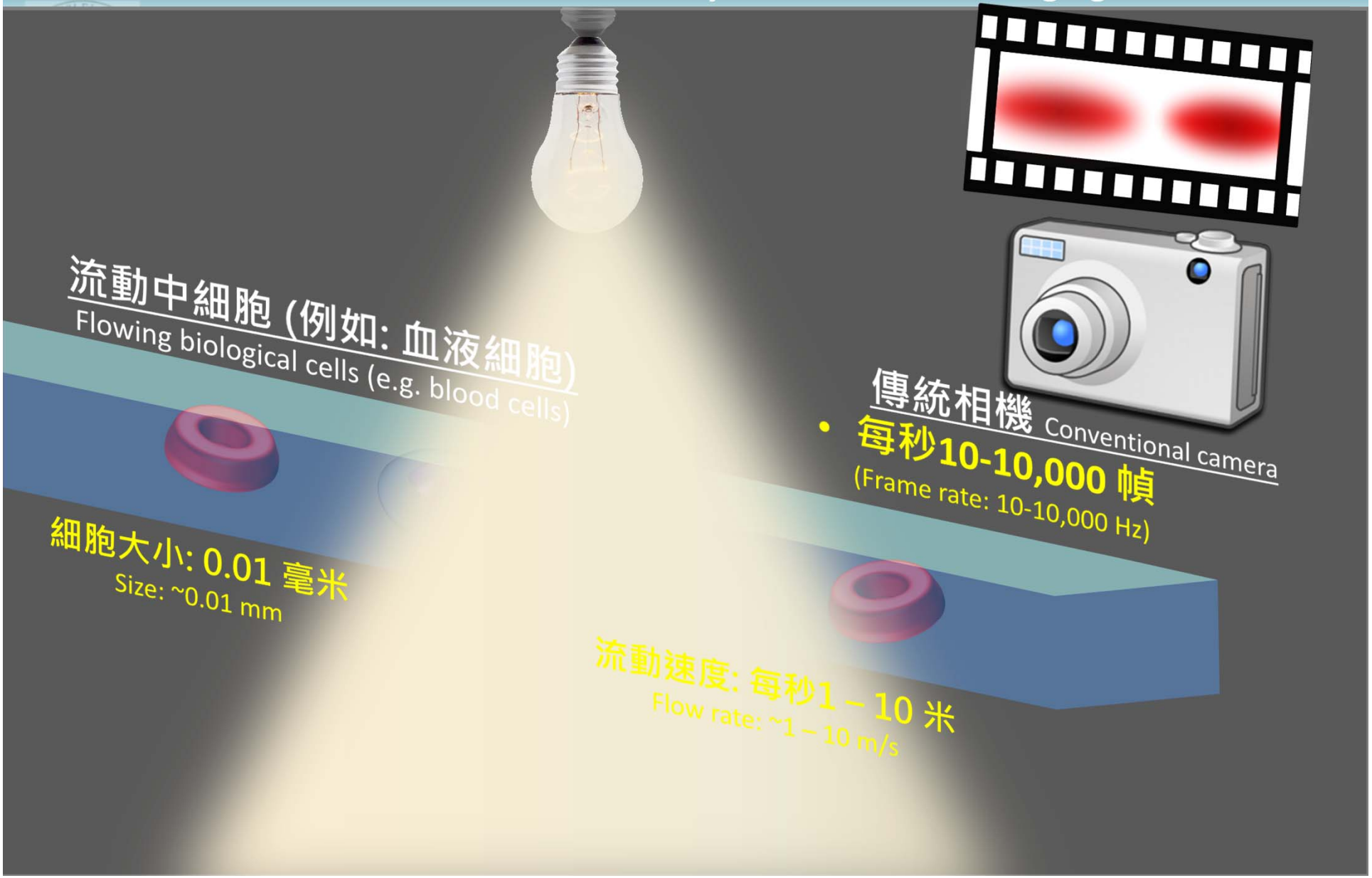
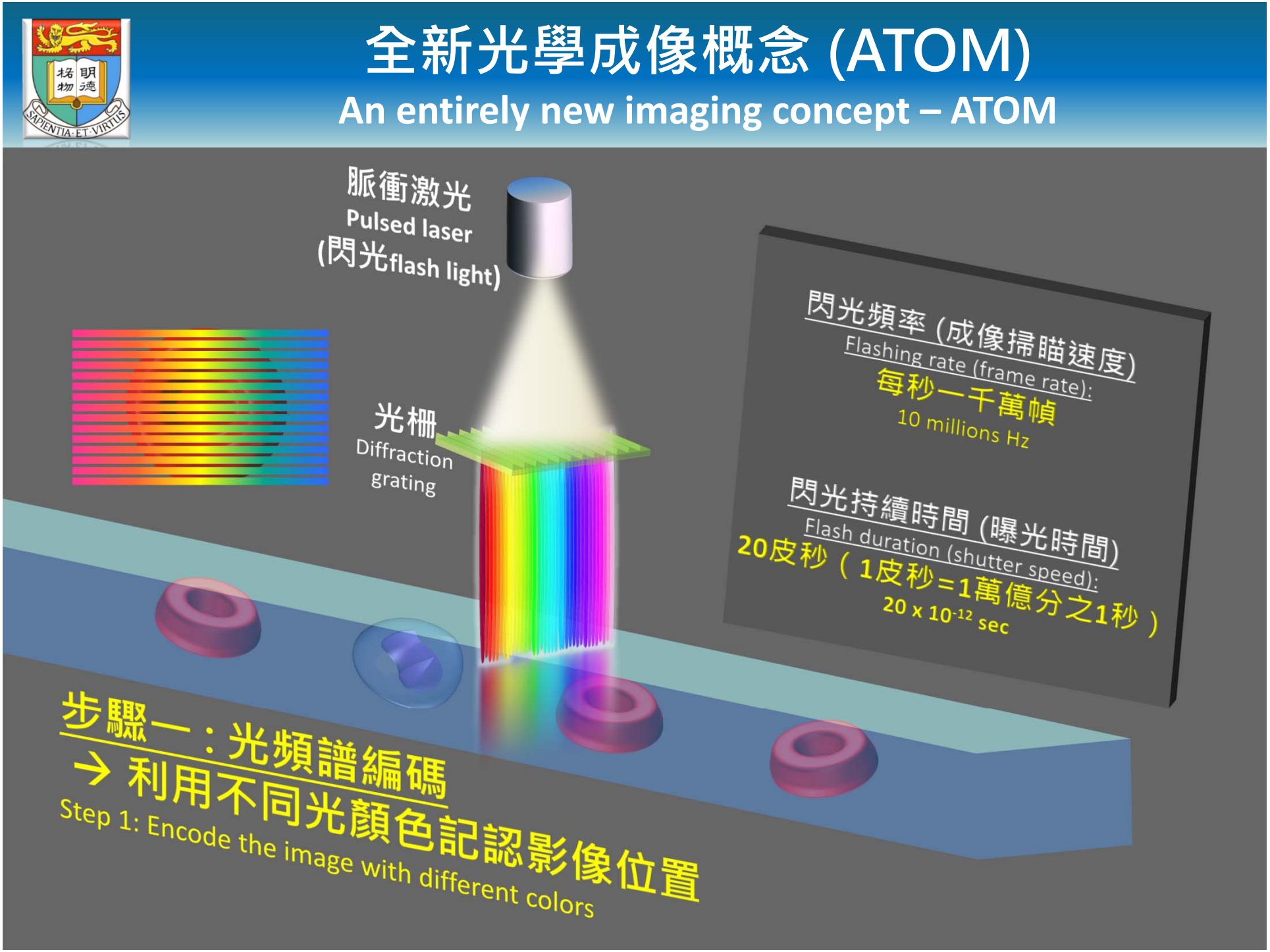
傳統拍攝/成像概念

What do we normally do when we do imaging?



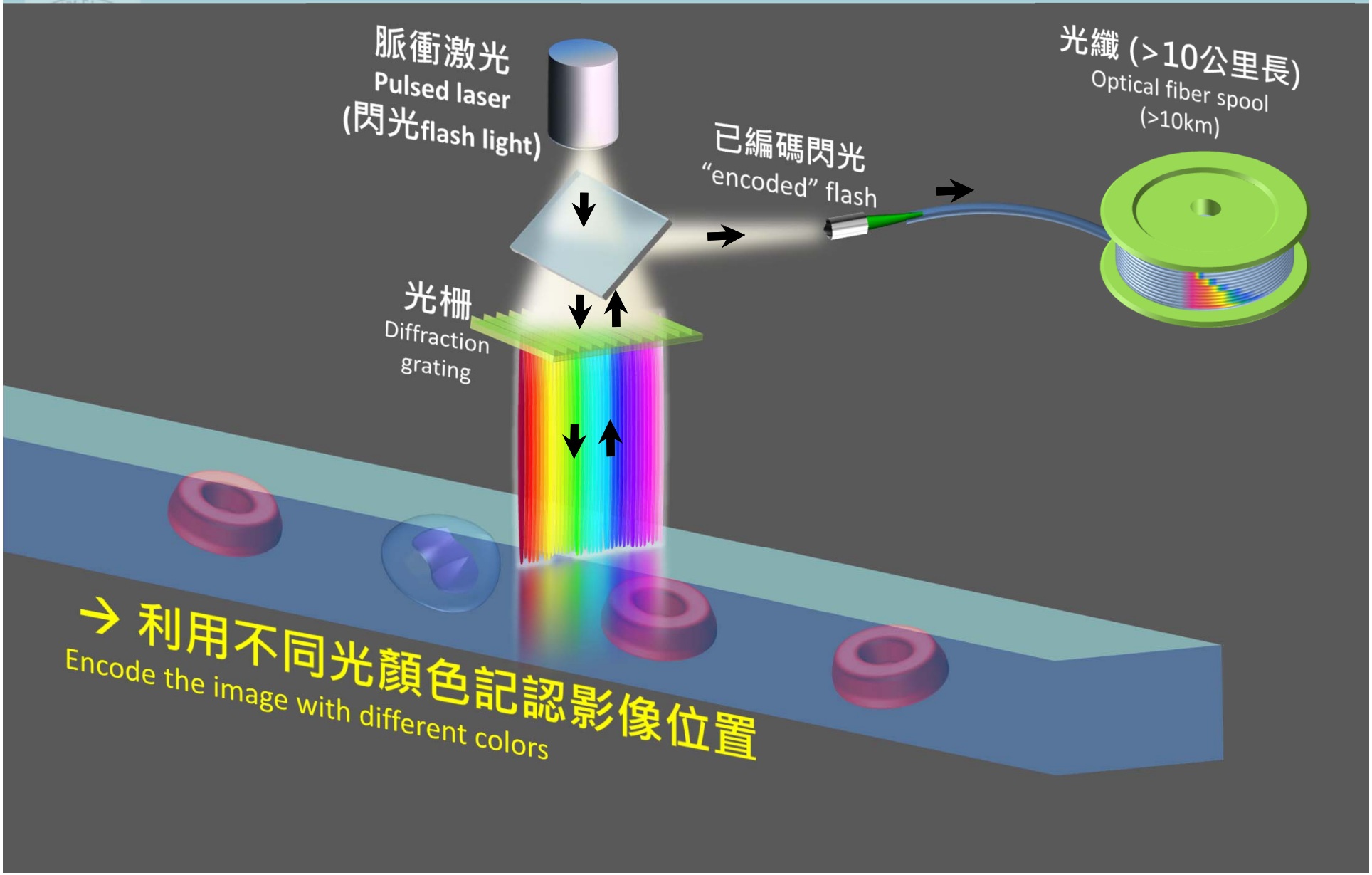
全新光學成像概念 (ATOM)

An entirely new imaging concept – ATOM



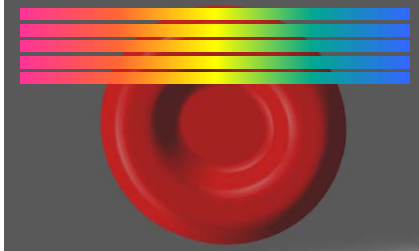
步驟一：光頻譜編碼

Step 1: Encode the image with different colors

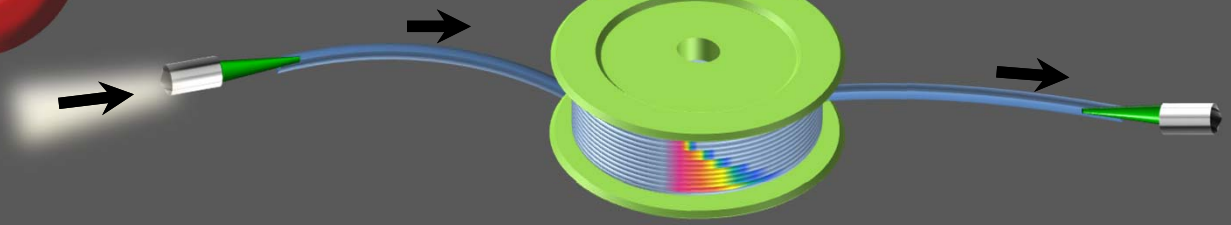


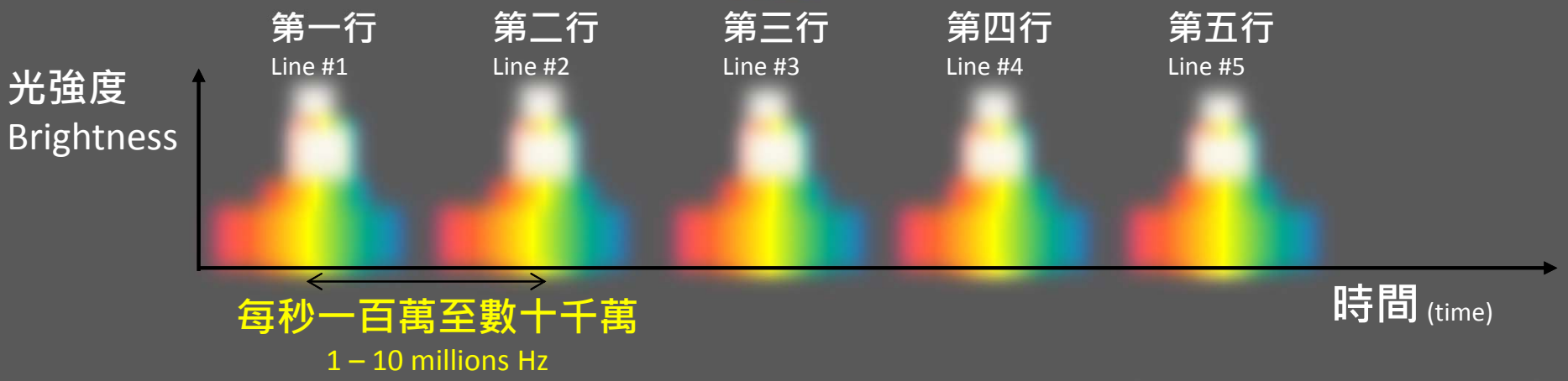
步驟二 :將光頻譜編碼轉化為時間編碼

Step 2: Wavelength-to-time mapping by stretching flash light (chromatic dispersion)

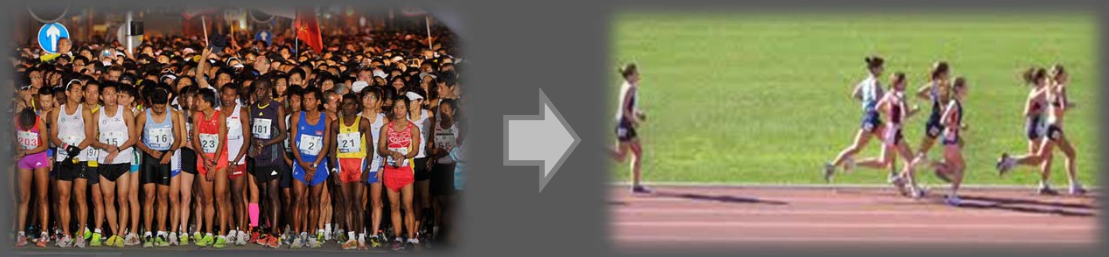


光纖 (>10公里長)
Optical fiber spool (>10km)





→ 利用色散現象



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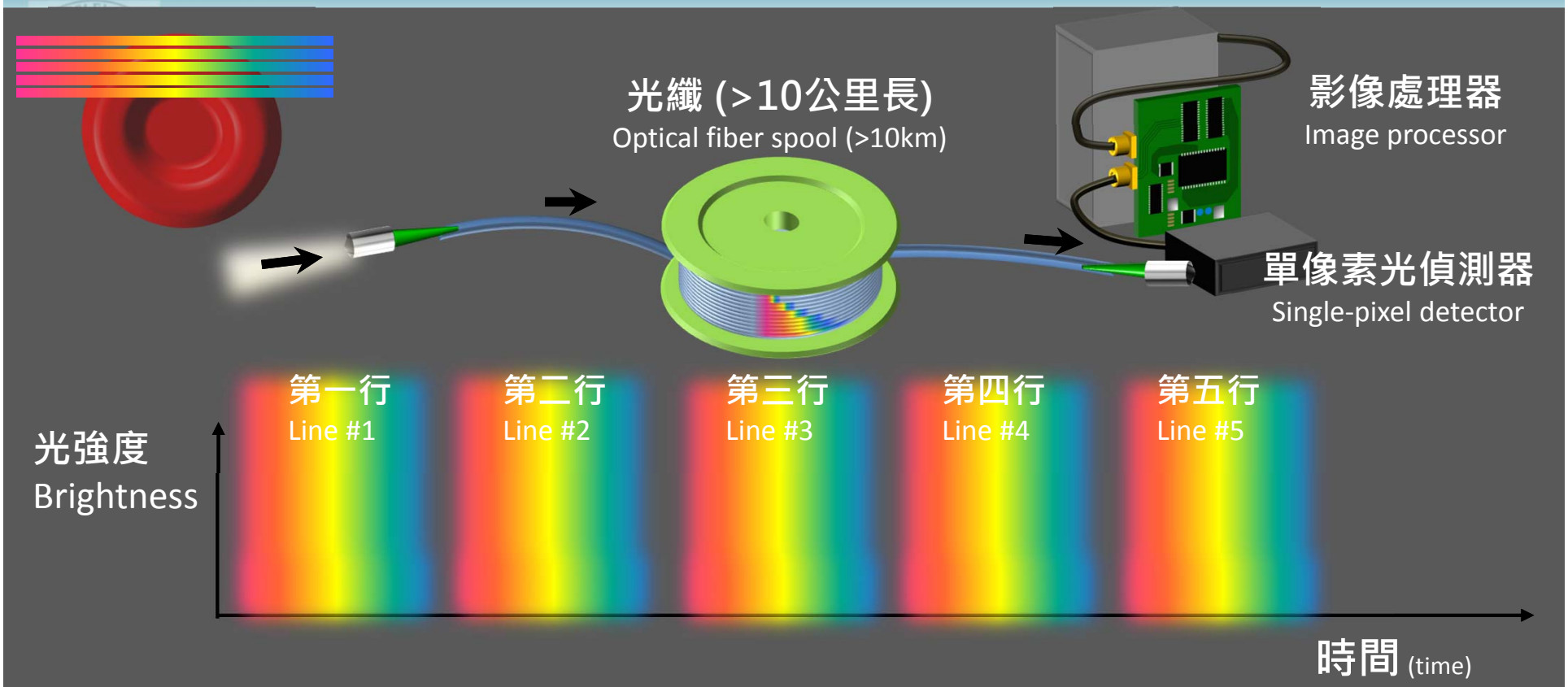


同時將被時間編碼的閃光強度增強

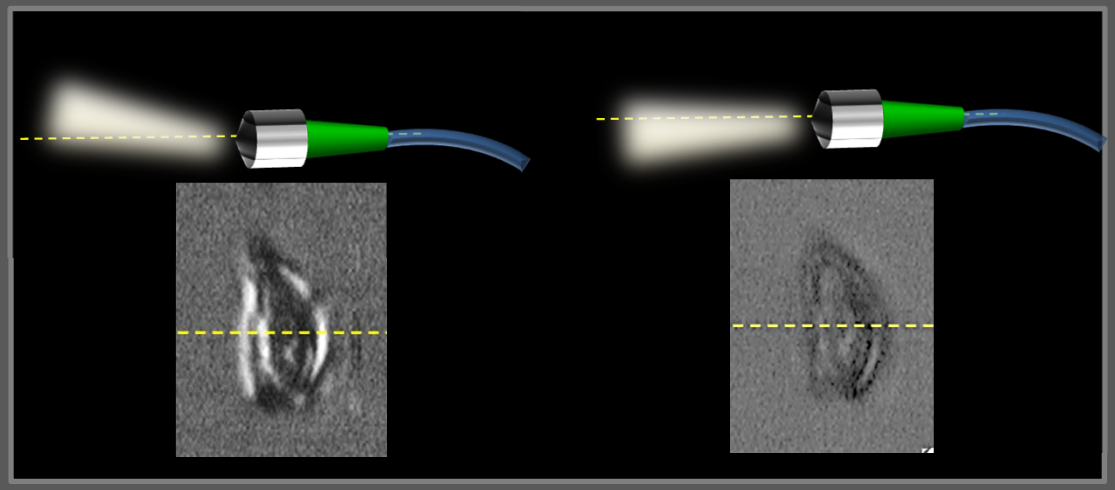
→ 打破現時影像感應器之限制 – 速度與敏感度之間的取捨

Optical amplification in the same fiber to obtain brighter image

→ overcome speed-versus-sensitivity trade-off!!

ATOM結合紋影成像 – 高速清楚拍攝透明細胞

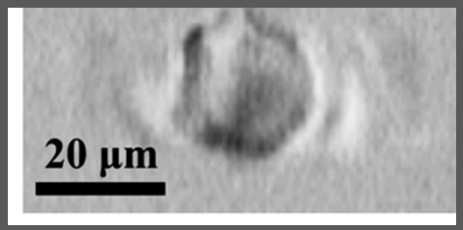
Modified Schlieren imaging – making transparent cells visible in ATOM



紋影成像

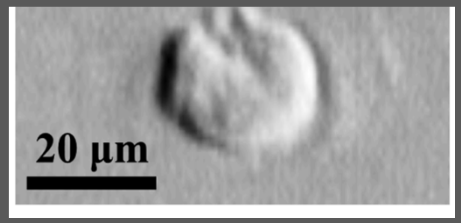
（Schlieren photography）

- 將光纖光學和激光技術結合常見攝影概念，稱”紋影成像”(Schlieren photography)
- 能超快速地清楚拍攝透明細胞及其內部結構
  (visualize the transparent cells at ultrahigh speed)
- 更能同時讀取影像的不同數據, 可用於診斷疾病之指標
  (Simultaneously obtain more image contrasts which can be indicators for diseases diagnosis)



細胞中光吸收度

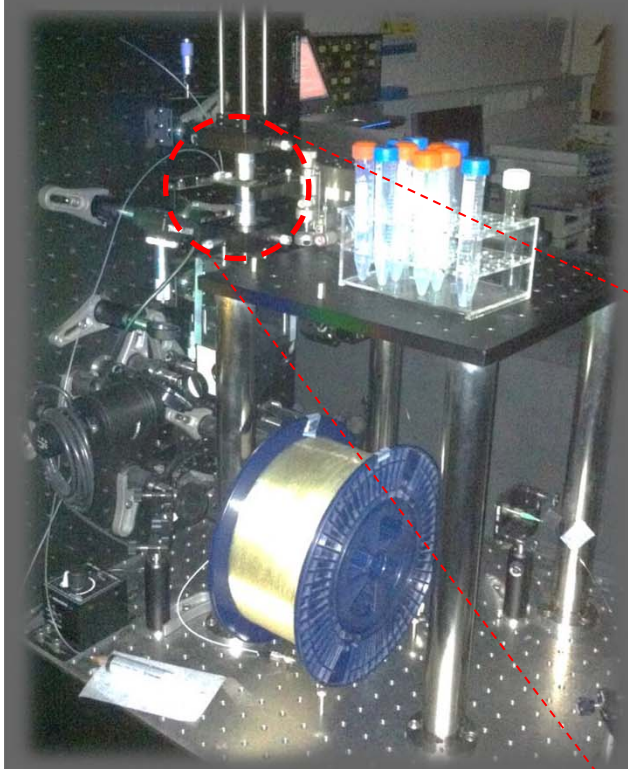
Absorption contrast

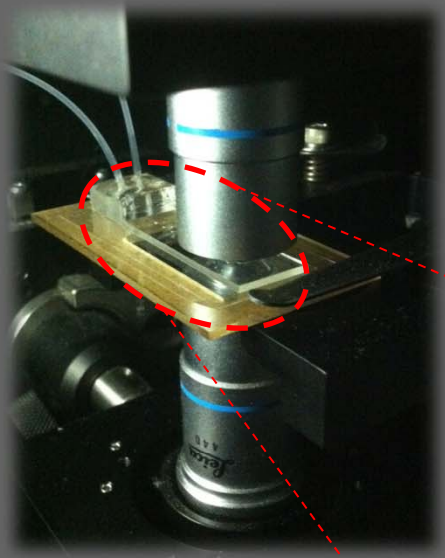


細胞中折射率

Gradient-phase contrast

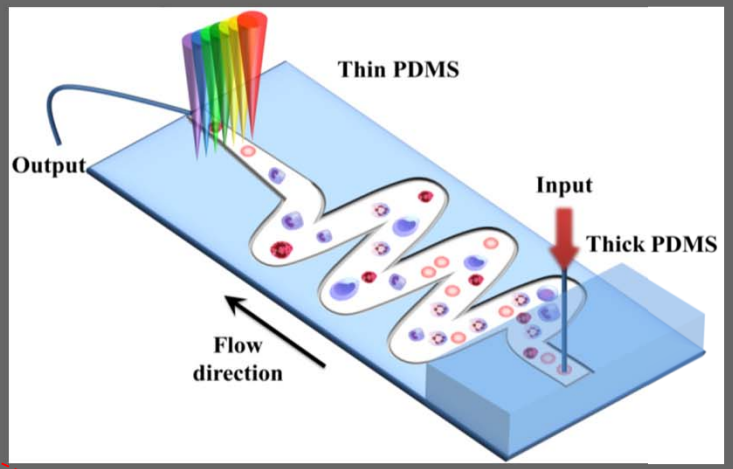
ATOM 系統
ATOM system

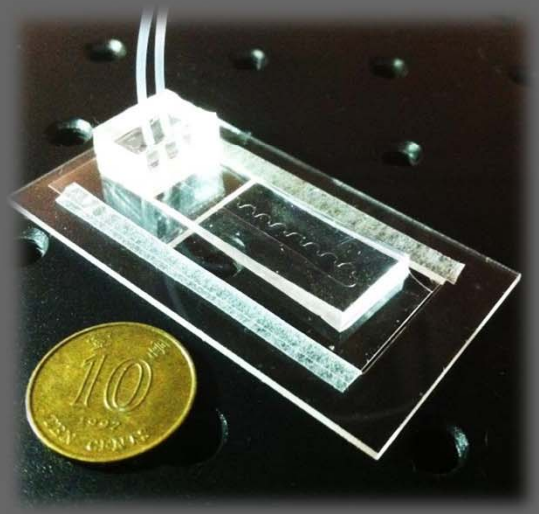




研製微流體晶片用作高速輸送細胞

In-house fabricated microfluidic chip for ATOM system



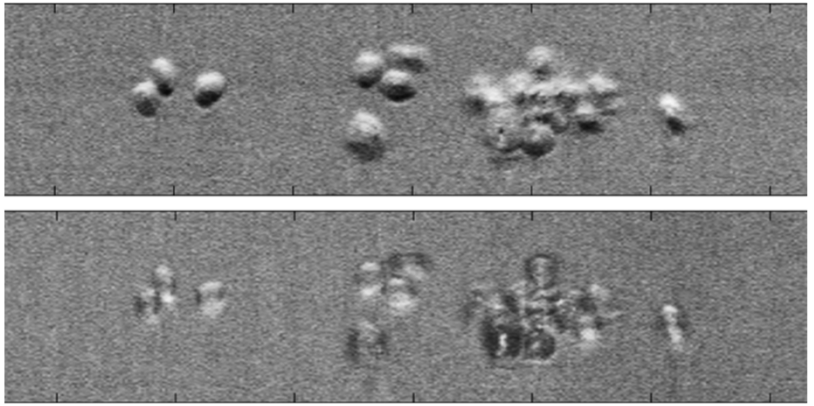


ATOM 與 高速 CMOS 相機之比較

ATOM vs high-speed CMOS camera

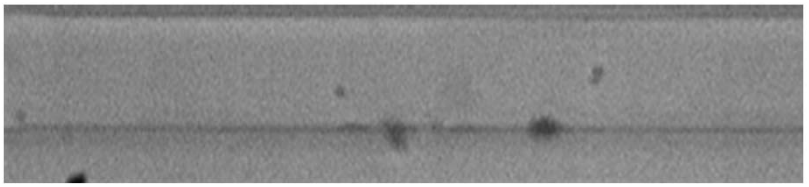
ATOM

- 成像掃瞄速度: 每秒二千六百萬
  Frame rate: 26 millions Hz
- **曝光時間: 20皮秒**
  Exposure time :~2**0 x 10^{-12} sec**
- **流速: 每秒十米**
  Flow speed: 10 m/s



CMOS 相機(CMOS camera)

- **成像速度: 每秒二萬三千**
  Frame rate : 23,000Hz
- **曝光時間: 0.001 毫秒**
  Exposure time: 0.001ms
- **流速: 每秒兩米**
  Flow speed : 2 m/s



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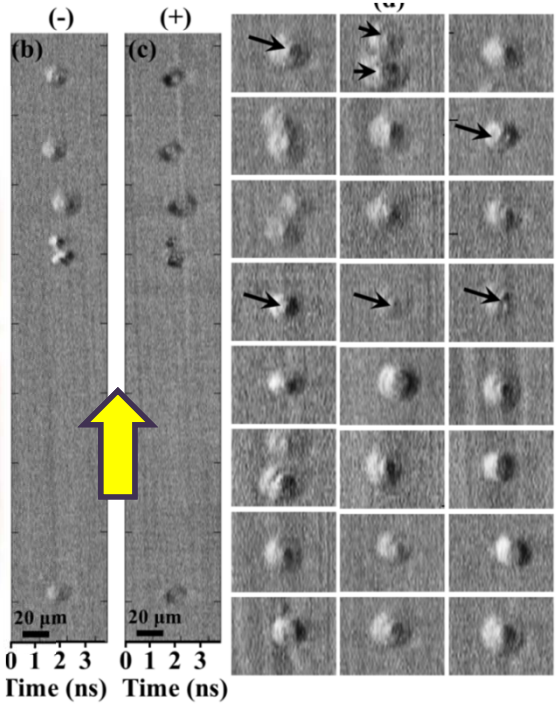
ATOM – 拍攝超高速流動血液細胞

Imaging blood cells in ultrafast flow

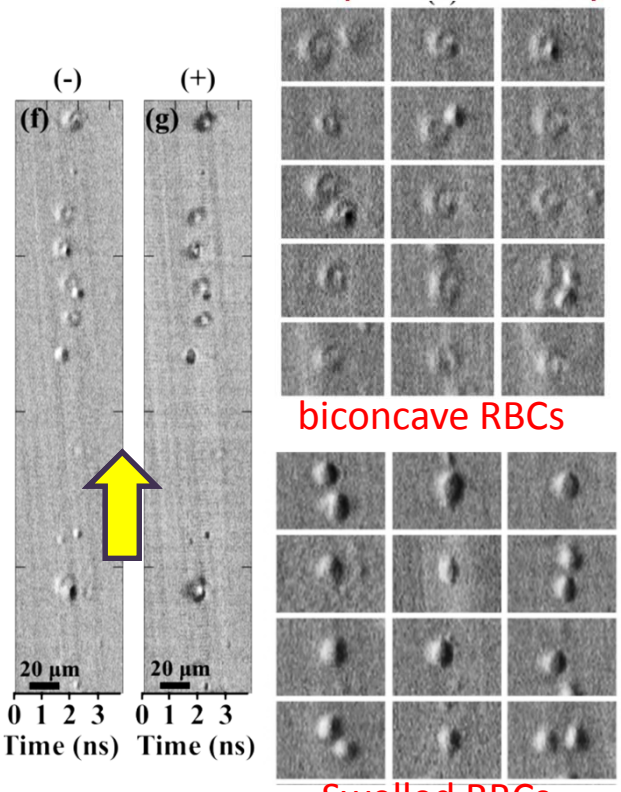
白血病细胞

leukemic monocytes



正常血液细胞 (紅血球)

Human whole blood (red blood cells (RBCs))



biconcave RBCs

Swelled RBCs

流速: 達到每秒十米 → 相等於每秒可拍攝十萬個細胞

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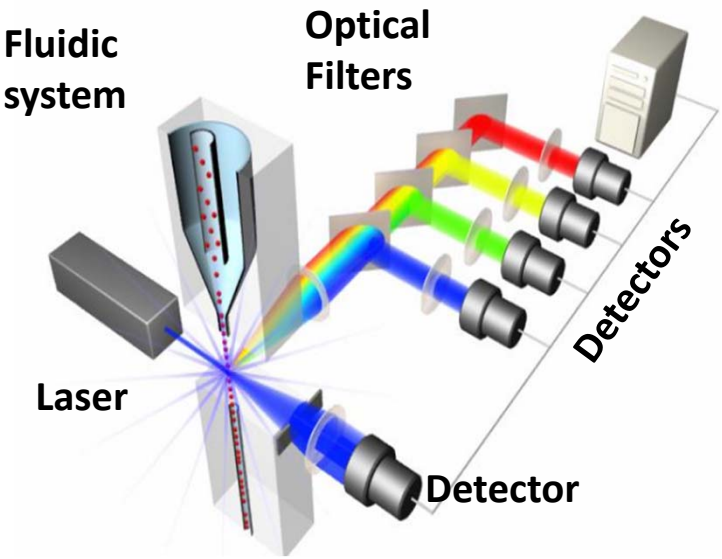
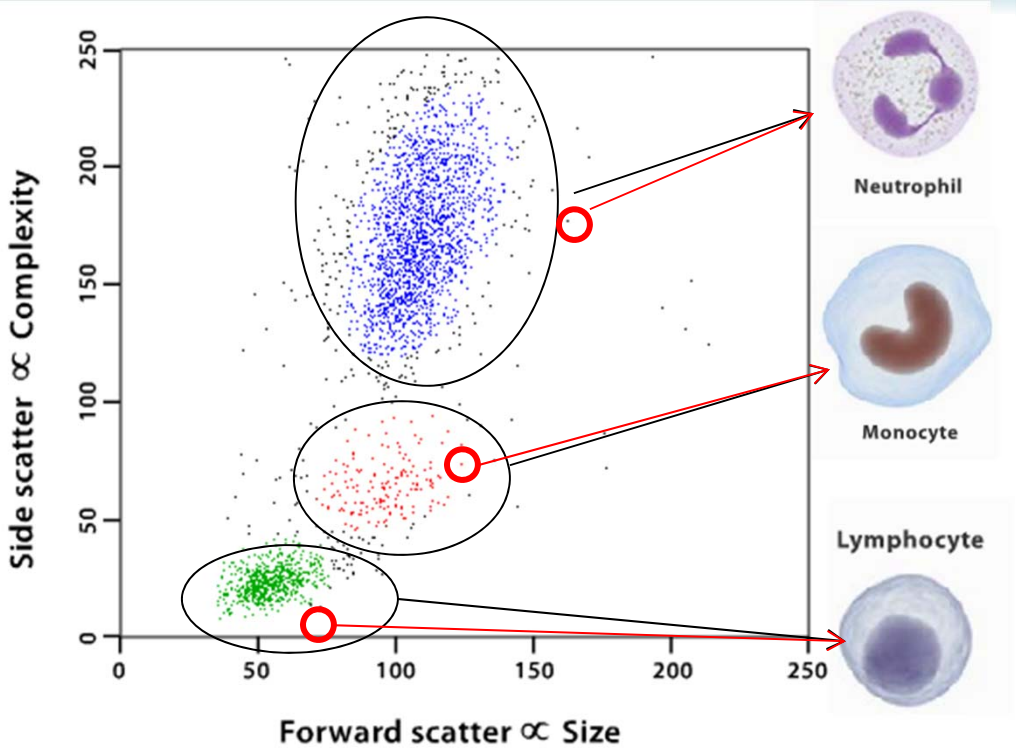
應用於高速「成像」流動細胞儀

ATOM for imaging flow cytometry



流速:每秒 1-4 米
Flow speed: 1-4 m/s
分析流量: 每秒> 5萬細胞
Throughput: > 50,000 cells/s

傳統流動細胞儀



ATOM - 「成像」流動細胞儀

- 影像分析流量達到每秒十萬個細胞
  Imaging throughput ~100,000 particles/sec
- 未有任何**CCD/CMOS影像感應器**技術可做到
  Not achievable by any CCD/CMOS cameras

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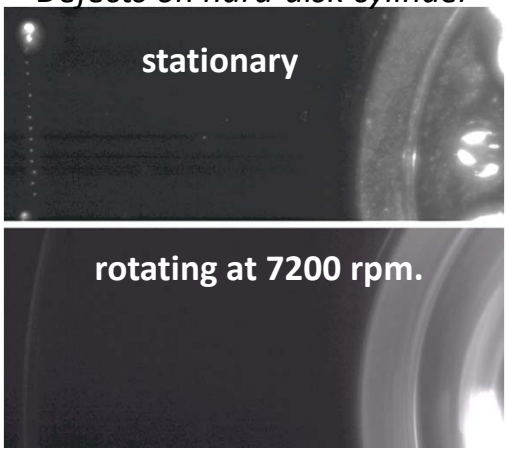
工業應用 –高速自動化品質監控

Industrial applications – automated quality control

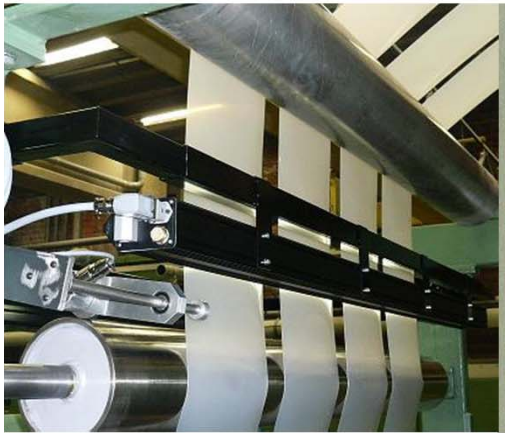
- **快速檢測物品表面的缺陷，於高速連續生產線上提供品質管控 (半導體片製造, 集成電路組裝, 印刷, 造紙業 等)**
  Surface inspection – a nondestructive evaluation method which is crucial for semiconductor wafer, paper, thin film production.

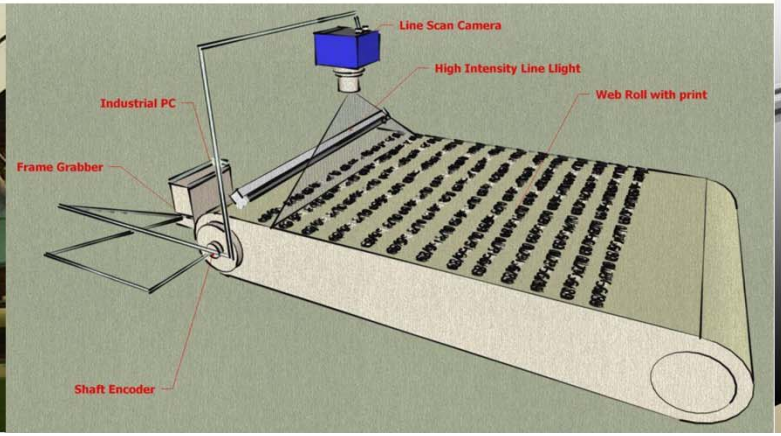
電腦硬盤碟上缺陷

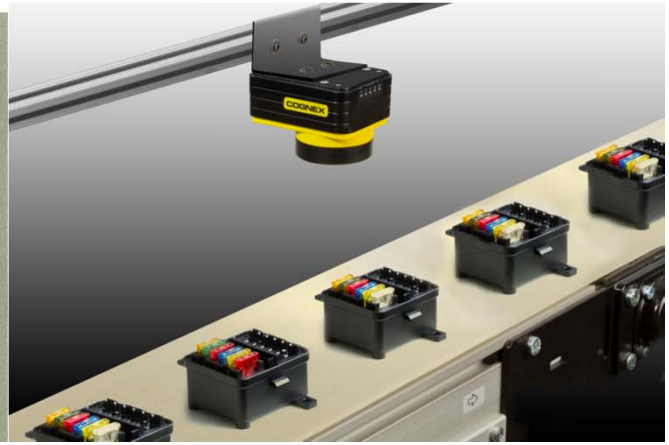
Defects on hard-disk cylinder



- **ATOM可快速 (每秒> 100 米) 檢測任何表面缺陷 (面積< 0.01 mm^2)**
  ATOM can easily locate defects with area <0.01 mm^2 (with the rolling speed > 100 m/s)







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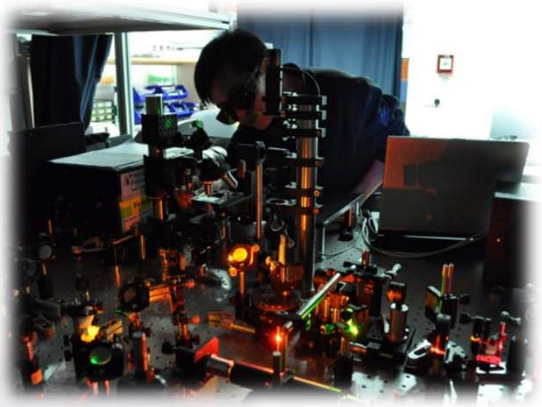

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