物理科學家如何跟活細胞玩：看一看及不只是看一看

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大綱

- 用甚麼工具看活細胞？
- 看活細胞要注意甚麼？
- 用甚麼工具能看得更清楚？
- 為什麼不能只是看一看？
- 用什麼工具可以不只是看一看？
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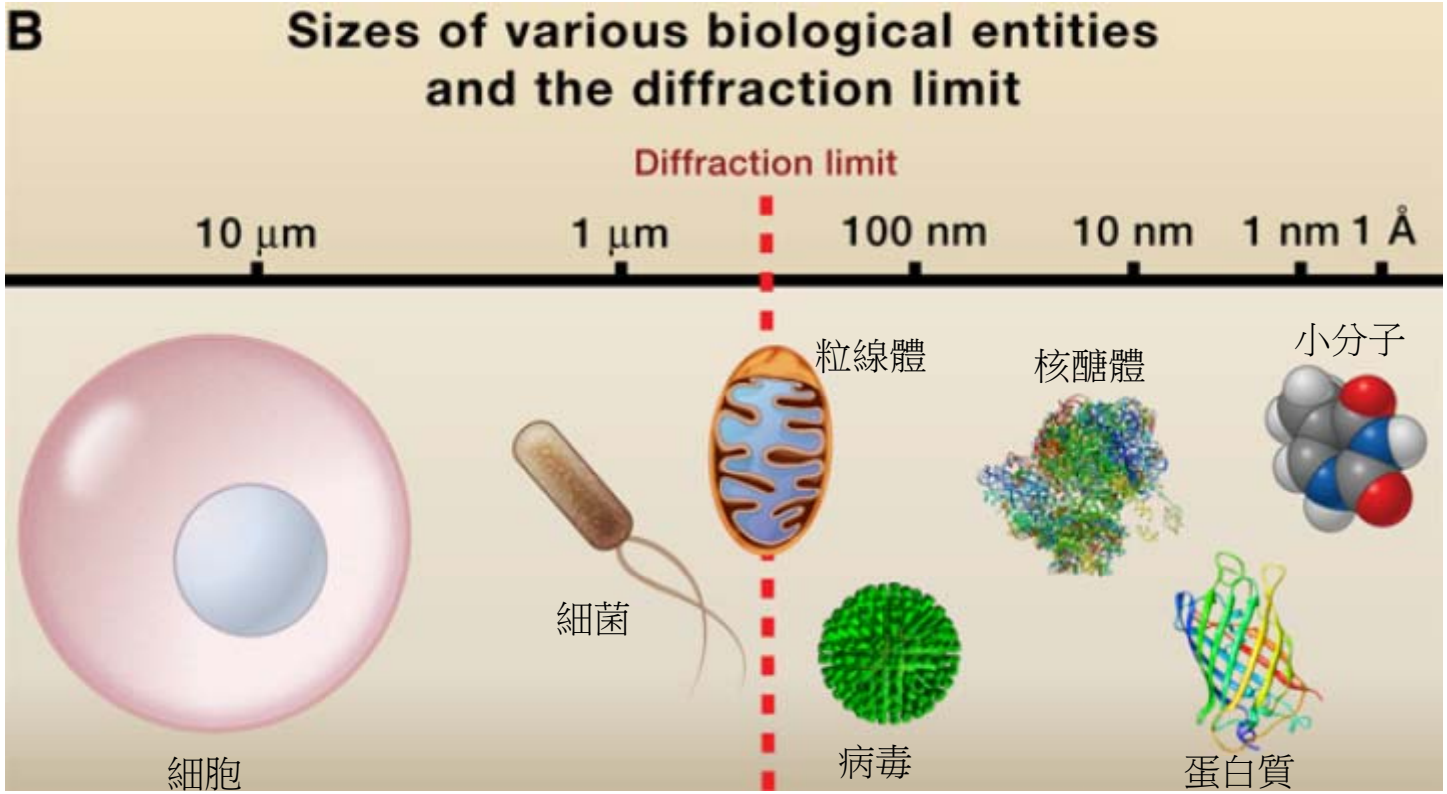
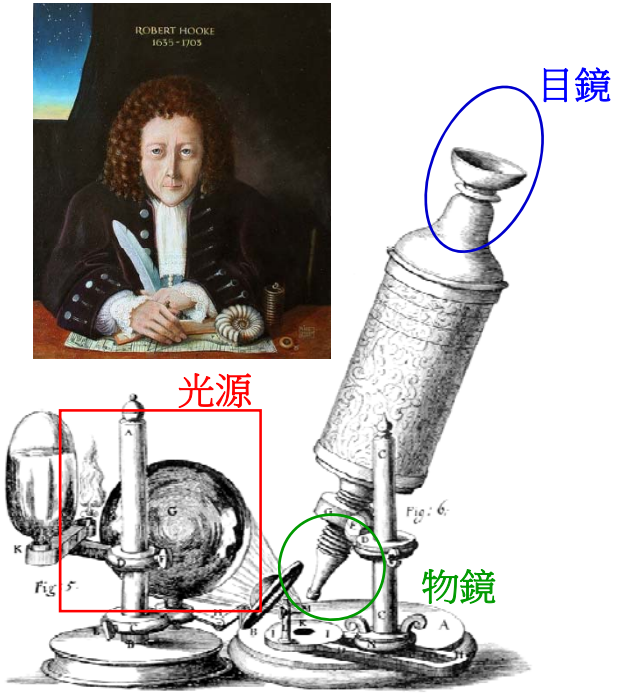
細胞的大小

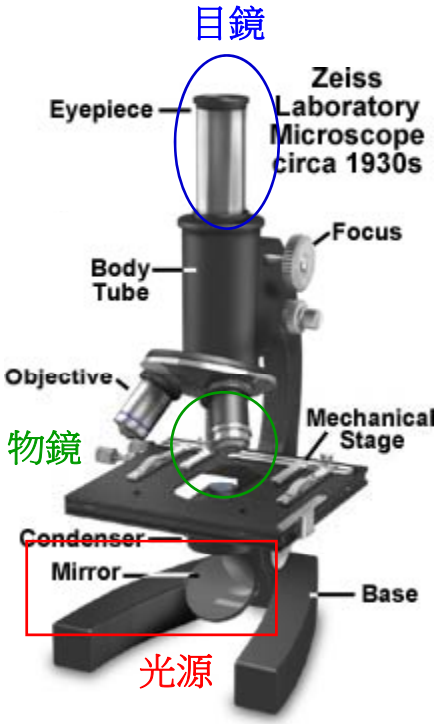


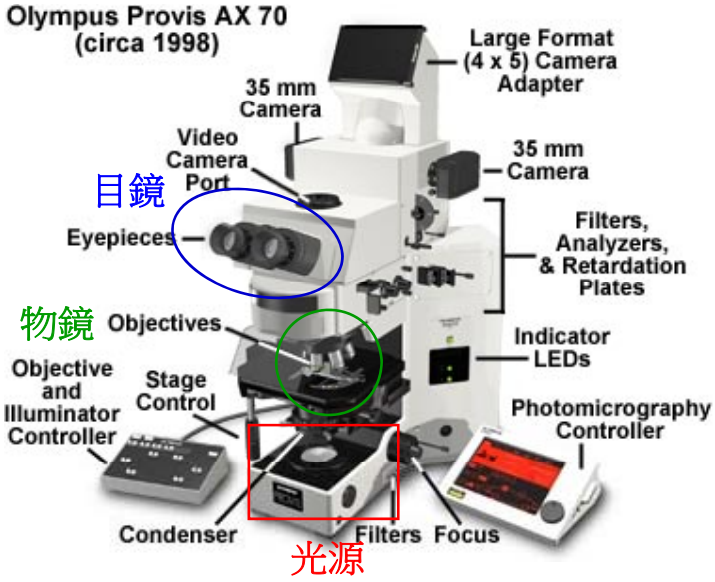
Ref: B. Huang, H. Babcock, and X. Zhuang, *Cell* **143,** 1047 (2010).

誰先看到細胞？用甚麼工具？



Robert Hooke, *Micrographia*, 1665

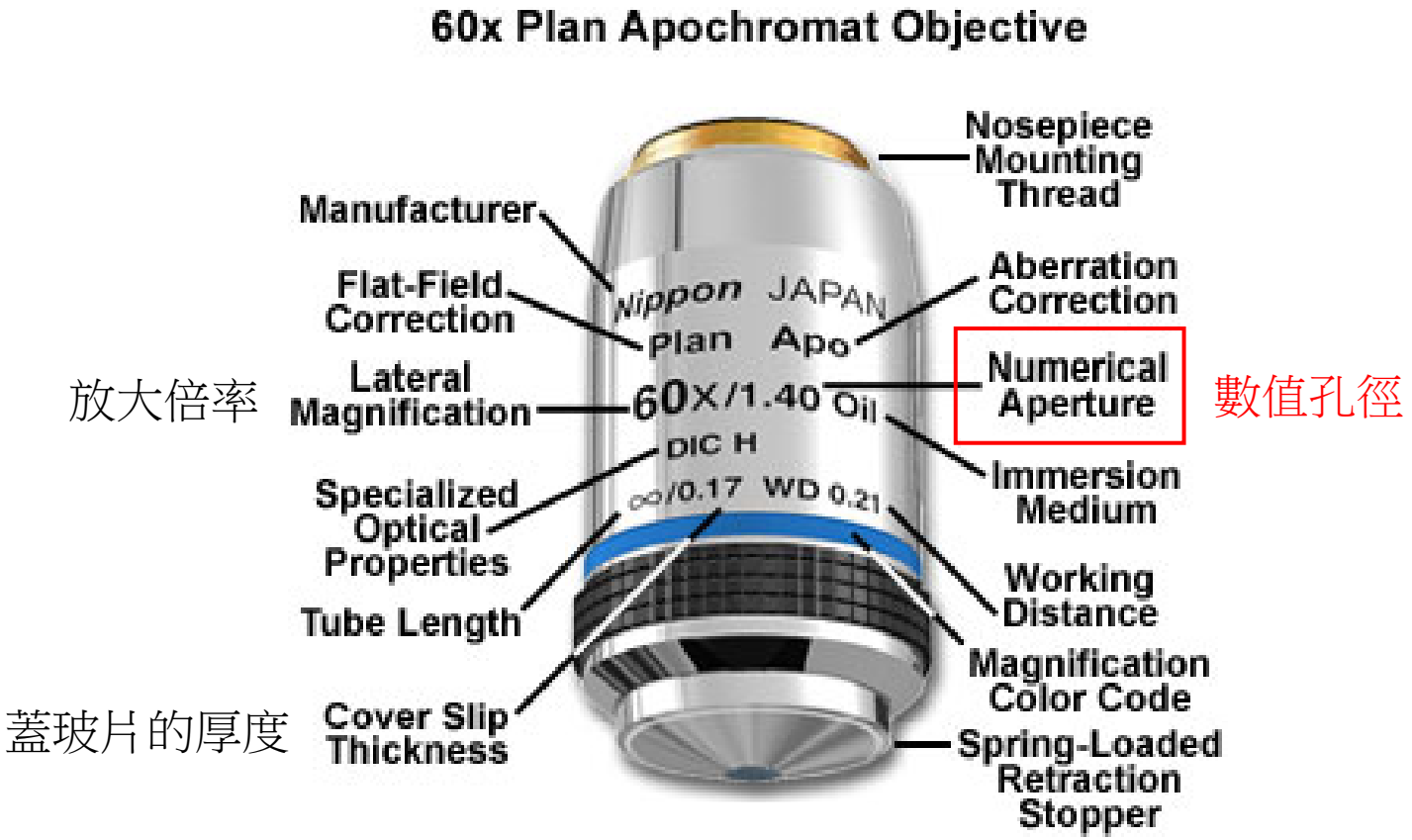




Images from *Wikipedia.*

Images from http://micro.magnet.fsu.edu/.

好的物鏡很重要...也很昂貴



Images from http://micro.magnet.fsu.edu/

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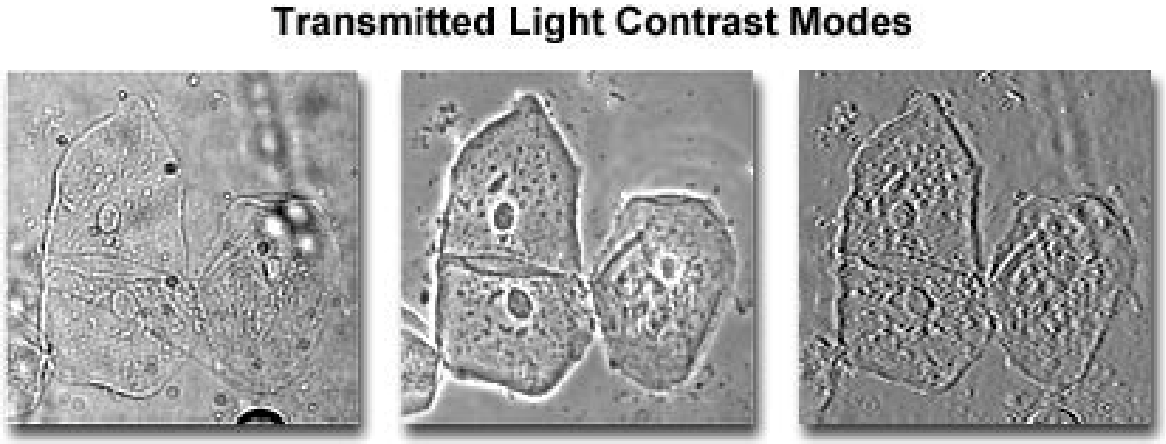
如何為透明的活細胞產生對比

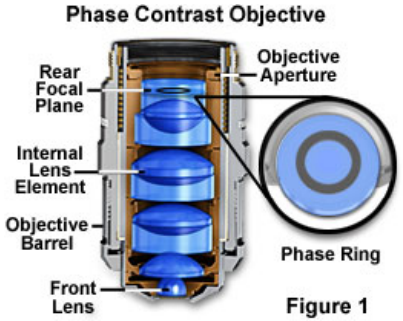


明視野影像

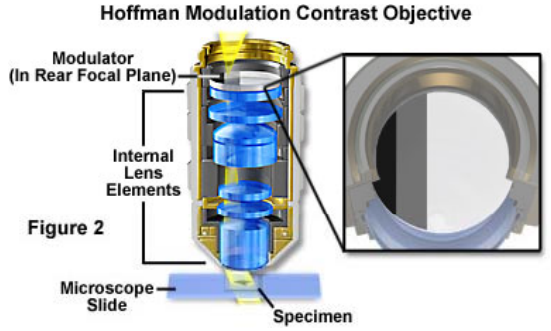
相位對比影像
(1953諾貝爾
物理獎)

Hoffman調制對比影像

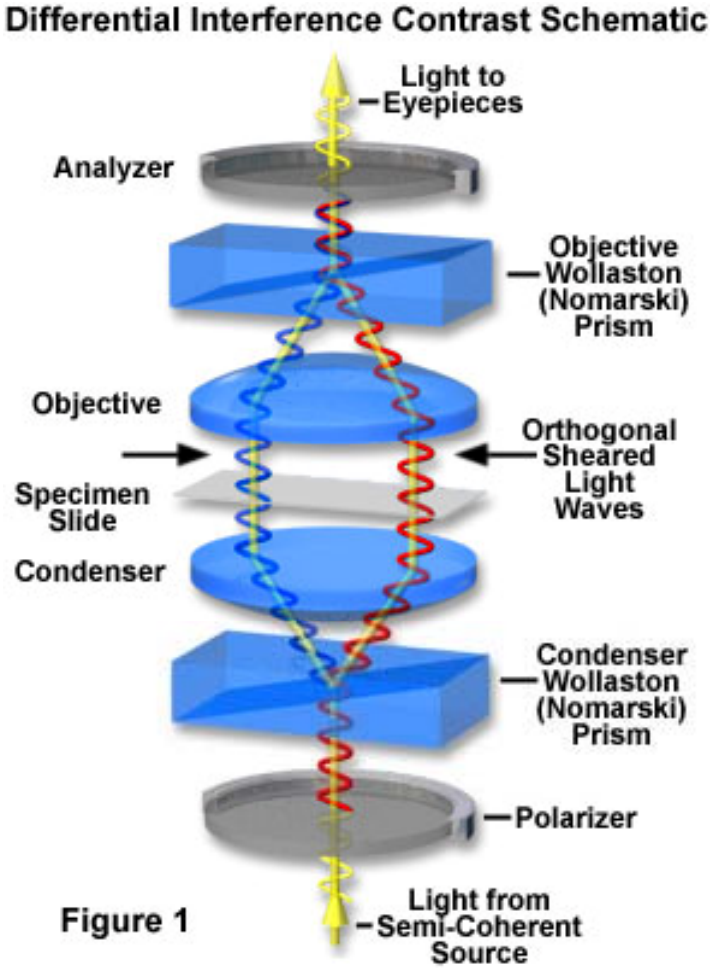
相位對比影像物鏡



Hoffman調制對比影像物鏡

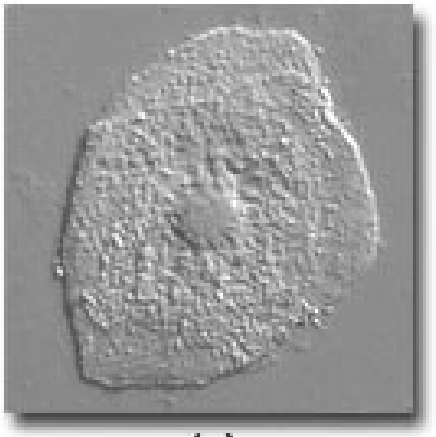


複雜的系統：微分干涉對比(DIC)

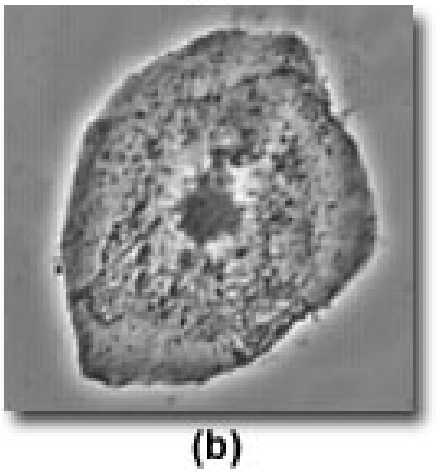


利用光的偏極化特性與干涉效應

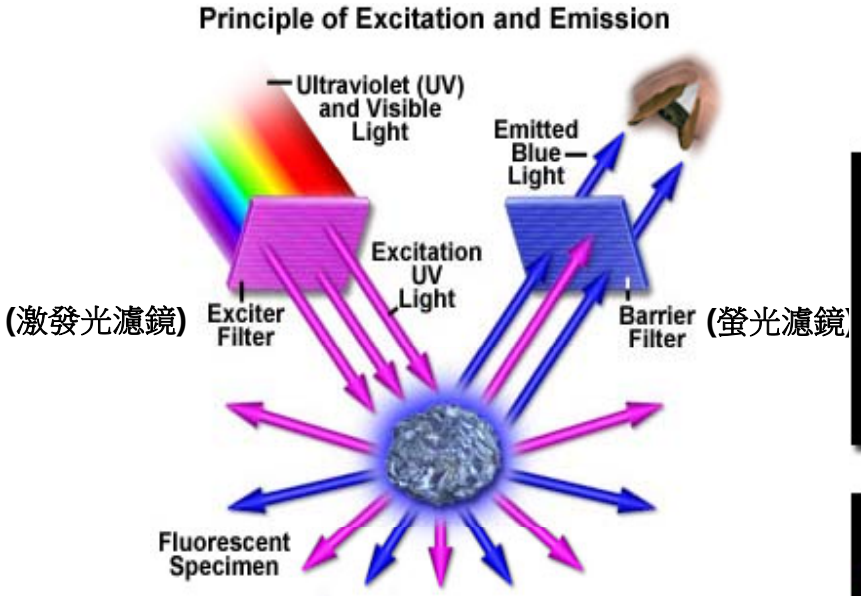
微分干涉對比影像



相位對比影像

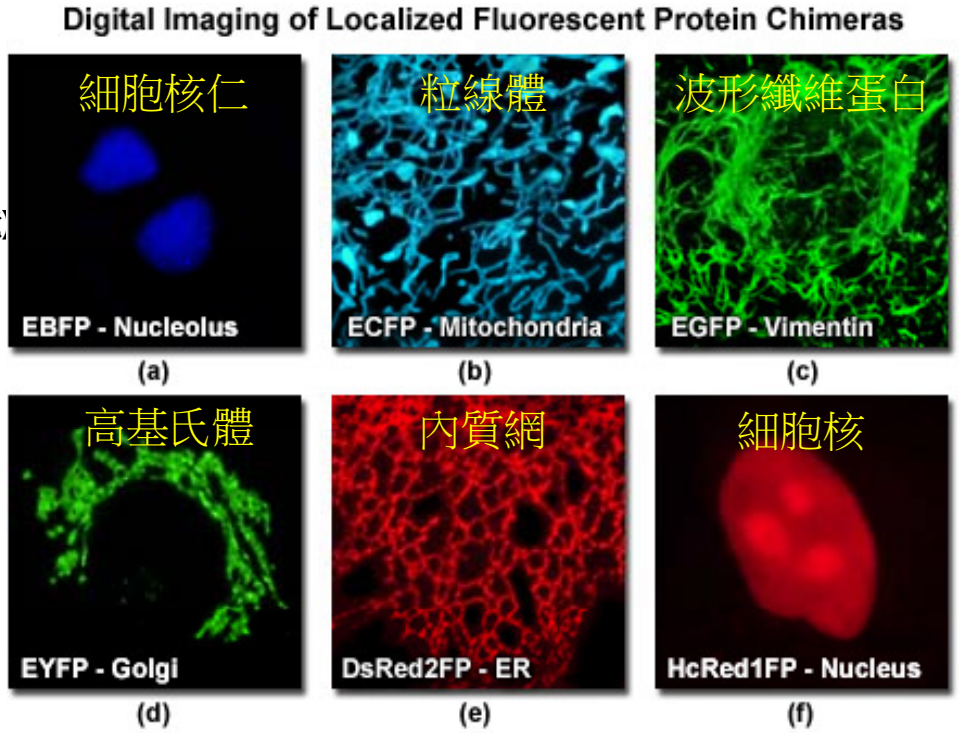


螢光染色對比



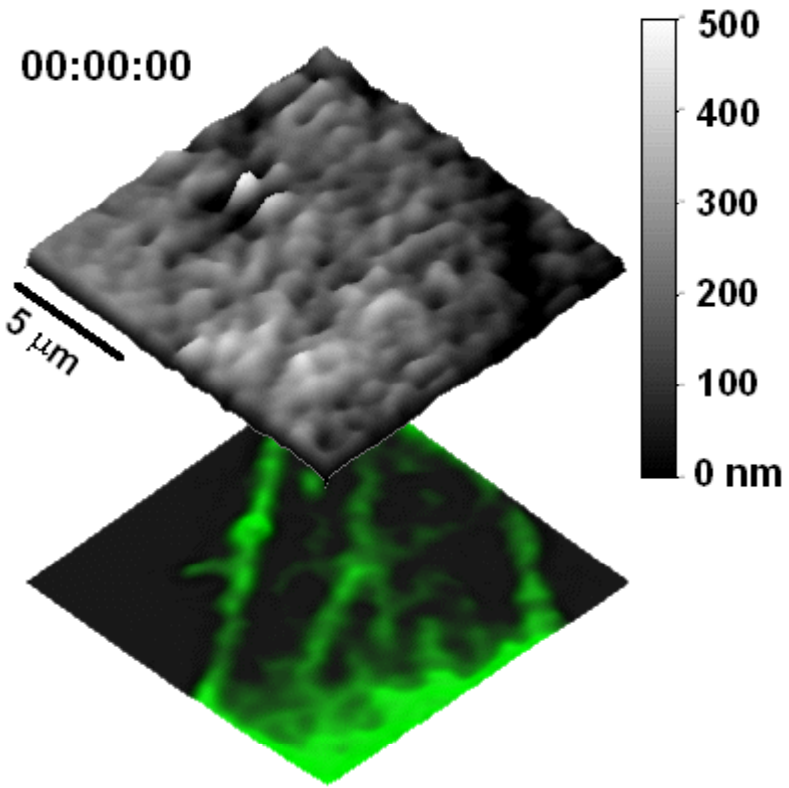
用一個較短波長的光源，激發細胞中會發出較長波長的螢光染劑、或者螢光蛋白。使用適合波長的濾鏡選出螢光訊號。

通常拍攝螢光影像的相機都是黑白的，取得影像後再用電腦加上想要的顏色。



Images are from http://micro.magnet.fsu.edu/

結合不同對比機制很有用



在此圖中我們用綠色螢光蛋白標定細胞中的肌動蛋白，用反射光與微分切片成像術做細胞膜與膜上微米小球的三維量測，因此可以計算出連結小球的肌動蛋白微絲的平移(~17 nm/min)及伸長速率(~8 nm/min)。

Ref: C.-C. Wang, J.-Y. Lin, H.-C. Chen, and C.-H. Lee, *Opt. Lett*. **31,** 2873 (2006).

細胞如果不高興，會死給你看

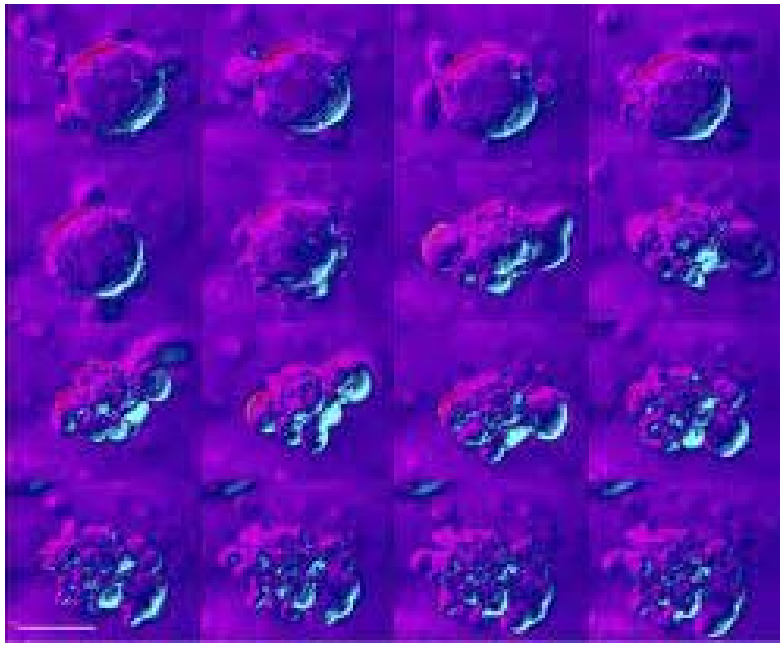


Image from http://www.sciencemuseum.org.uk/

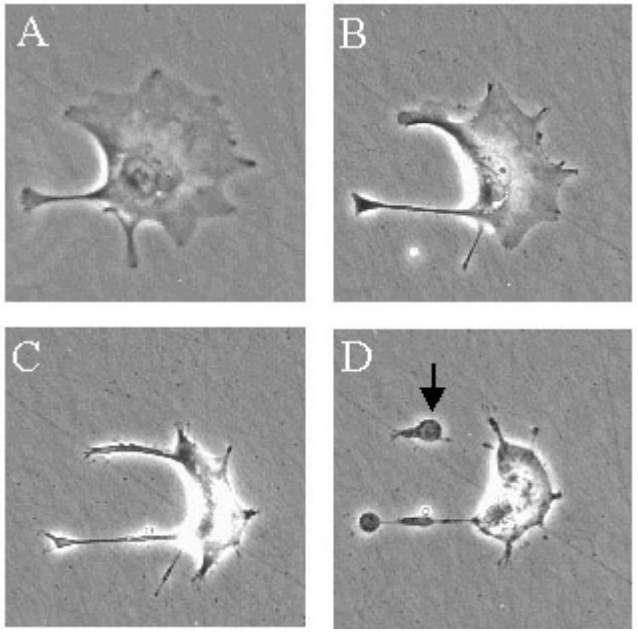
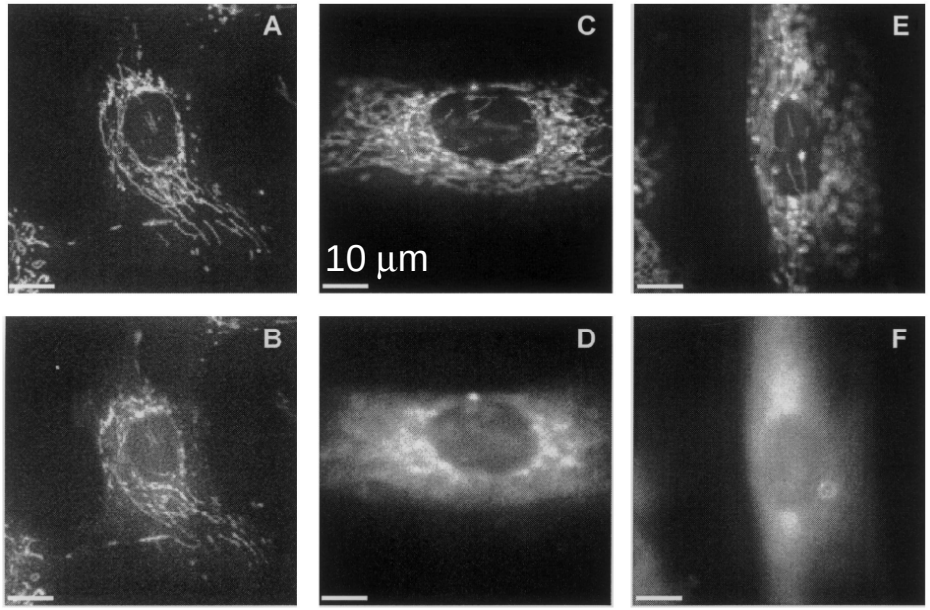


Image from http://www.rcdrg.sgul.ac.uk/

降低光毒性對活細胞觀測很重要

光毒性主要來自對細胞中的粒線體的破壞；受到紫色或藍色的光線照射後，在粒線體附近會產生大量的活性氧(reactive oxygen species)自由基，造成粒線體膜分解。



Ref: G. Ouedraogo et al., *J. Photochem. Photobiol. B* **58,** 20 (2000).

如何降低光毒性：

- 擋掉光源中的紫外光
- 減少曝光時間
- 使用黃色或紅色的染劑
- 使用減少氧溶解量的藥劑，例如Oxyrase
- 使用隔絕空氣的培養系統，或在培養液表面滴油

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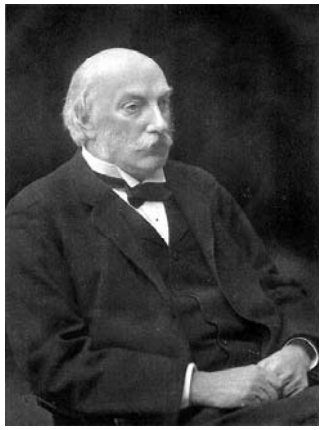
光學解析率有極限

對顯微鏡而言，橫向解析率由光波長(λ)和物鏡的數值孔徑(NA)決定。



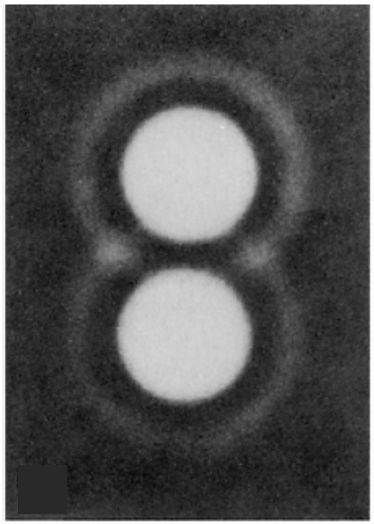
Lord Rayleigh
(1904諾貝爾物理獎)

Rayleigh criterion:

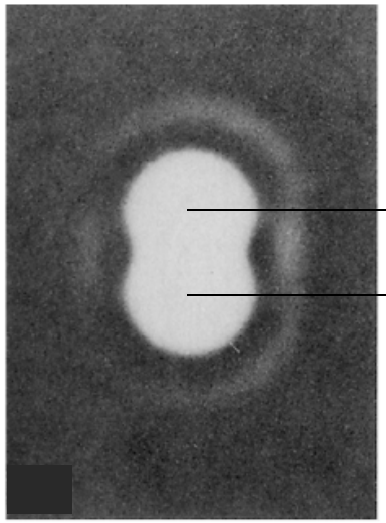
橫向解析率 ~ 0.61λ /NA

乾物鏡, NA < 1.0

浸油物鏡, NA < 1.5



可解析



可解析的極限

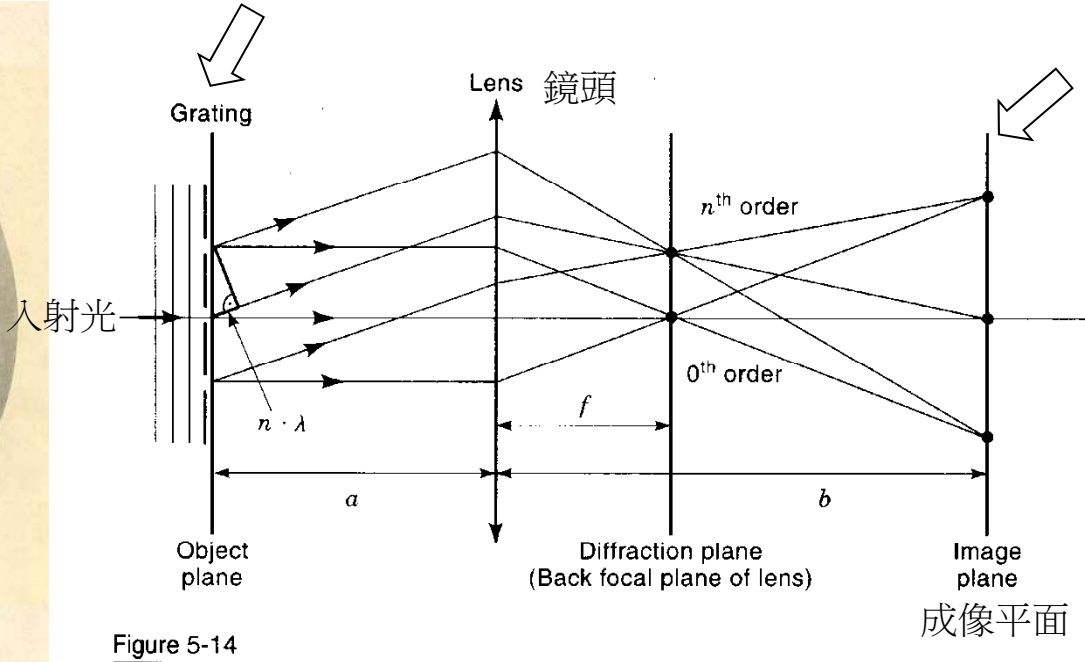
在可見光波段，橫向解析率的極限大約是250 nm.

Ref: M. Born and E.Wolf, *Principles of Optics*, 6th ed. (Pergamon, Oxford, 1980), Chap. 8.

Abbe的成像理論

樣本的繞射(diffraction)作用，使光偏折一個角度。

Ernst Abbe, 1840-1905



在像平面上，不同角度的光經過透鏡聚焦後，互相干涉而形成影像。

成像公式

$$\frac{1}{a}+\frac{1}{b}=\frac{1}{f}$$

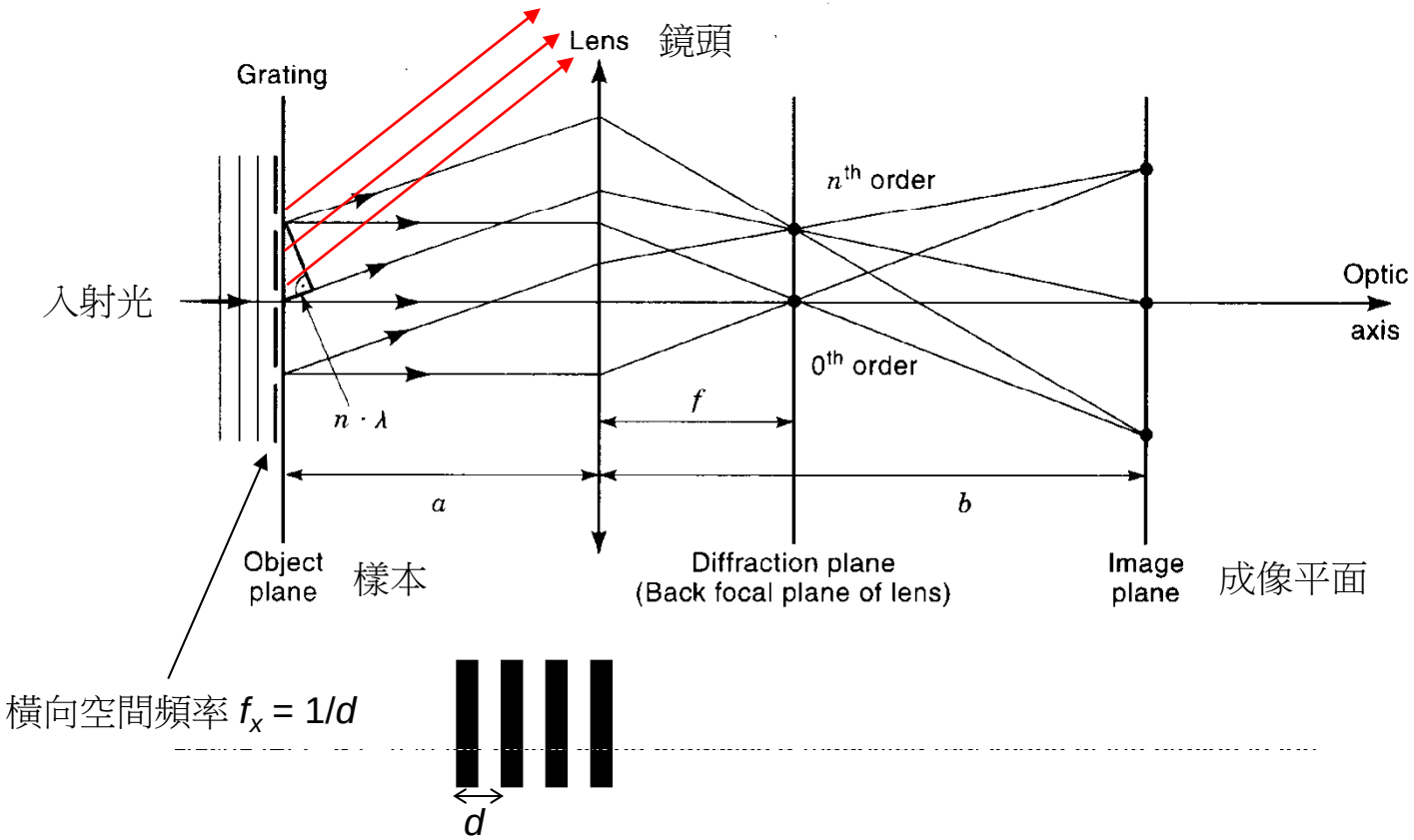
Figure 5-14

Abbe's theory for image formation in a light microscope. An objective lens focused on a grating ($2f > a > f$) in the object plane produces a magnified real image of the grating in the image plane. The diffraction plane is located at $1f$ in the back aperture of the lens. An incident planar wavefront is shown. Diffracted nth-order and nondiffracted 0th-order rays are separated in the diffraction plane, but are combined in the image plane.

Ref: D. B. Murphy, *Fundamentals of Light Microscopy and Electronic Imaging* (Wiley-Liss, New York, 2001).

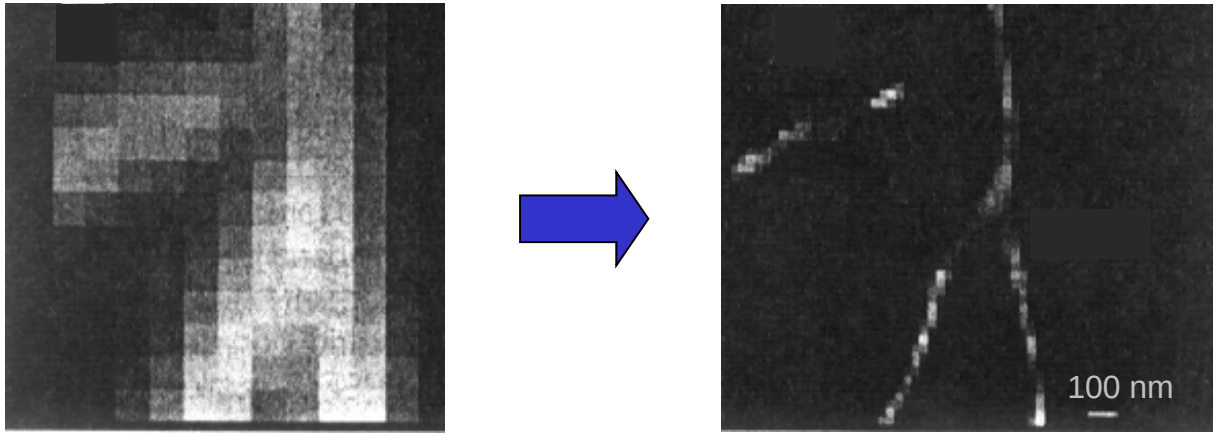
光學解析率極限的物理機制

樣本的細微部分，又叫高空間頻率的成分，將使經過樣本的光偏折很大的角度。角度過大而無法被鏡頭收集的成分，就不會出現在影像上。鏡頭最大收集光角度如果是θ, 則數值孔徑 NA=*n**sin θ。其中*n*是鏡頭周圍空間的折射率。



電腦可以把影像算回來

因為成像過程完全是可以用數學公式描述的，如果影像的對比度夠高（即雜訊夠小），我們可以在電腦上模擬成像的過程，然後把拍到的影像當成結果，「猜」出一個最有可能的原始樣本形狀。



樣本：細胞中的微管絲(microtubule)

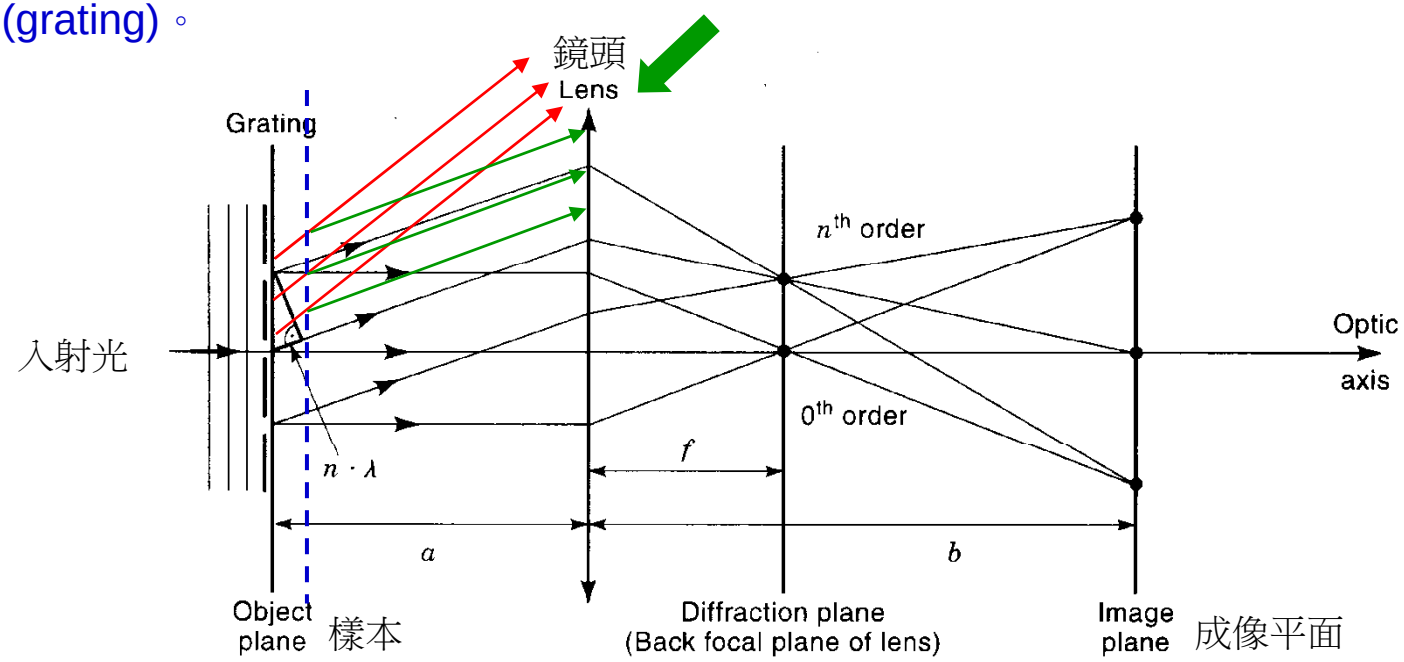
經過大約2000次的遞迴運算，可達到接近50奈米的橫向解析率。

Ref: W. A. Carrington *et al*., *Science* **268,** 1483 (1995).

結構式照明可提高橫向解析率

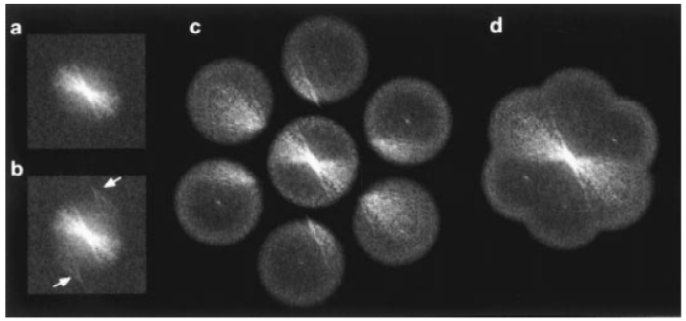
在樣本上另外投影一個週期性光圖樣，形成一個光柵(grating)。

光柵會將原本不能進入鏡頭的光線再次偏折，使它有可能進入鏡頭。因此本來不能成像的部分也會成像。

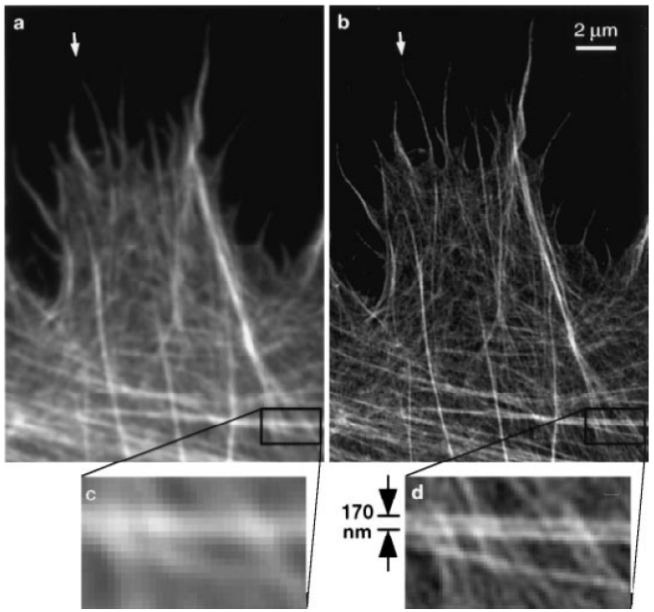


結構式照明顯微術：拍很多張，組回一張

空間頻率成份



為了要照顧到各個方向的大角度影像成分，以及計算出完整影像所需，每張畫面需要9張有結構的照明的影像，才能組回1張。

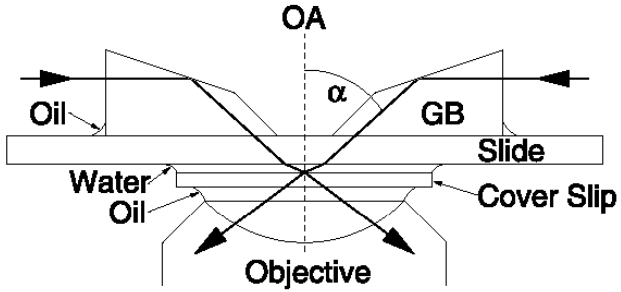


橫向解析率可達到~$\lambda/4$.

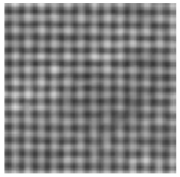
Ref: M. G. L. Gustafsson, *J. Microsc*. **198,** 82 (2000).

不同的演算法，可以減少拍攝的張數

Harmonic excitation light microscopy (HELM)



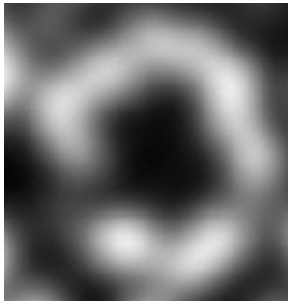
利用4道雷射光干涉
造成的結構式照明



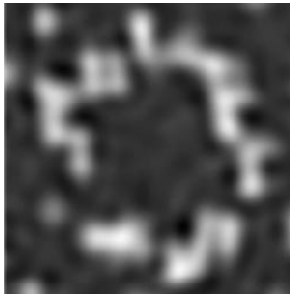
$$\tilde{\theta} = T \times (4A + e^{i\Delta_x}B^{+} + e^{-i\Delta_x}B^{-} + e^{i\Delta_y}C^{+} + e^{-i\Delta_y}C^{-}).$$

用5張就可組回一張

100 nm螢光小球



一般螢光影像



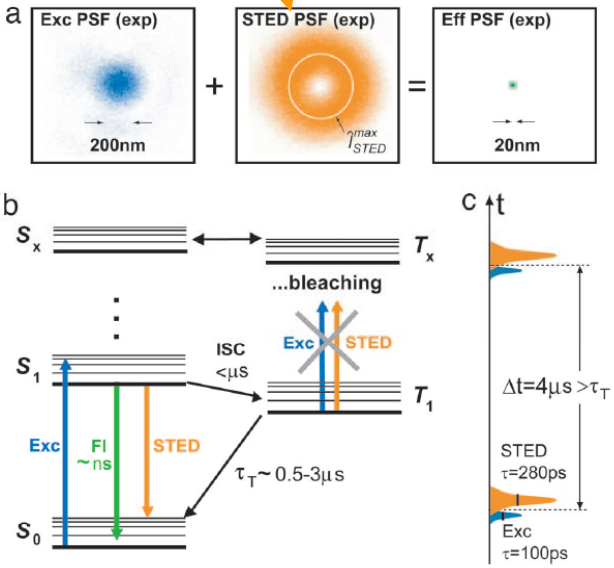
HELM影像

Ref: J. T. Frohn, H. F. Knapp, and A. Stemmer, *Proc. Natl. Acad. Sci. USA* **97,** 7232 (2000).

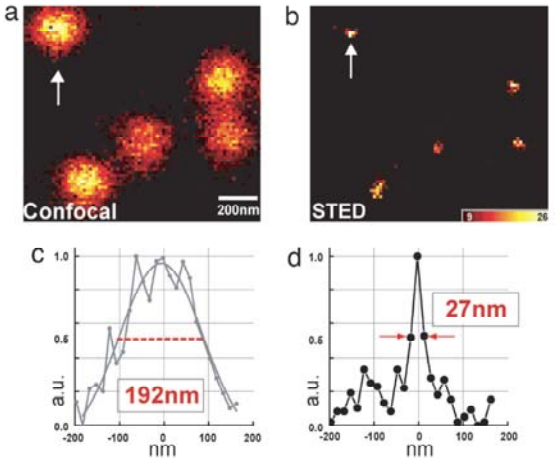
受激發射耗乏Stimulated emission depletion (STED)顯微術

Stefan W. Hell

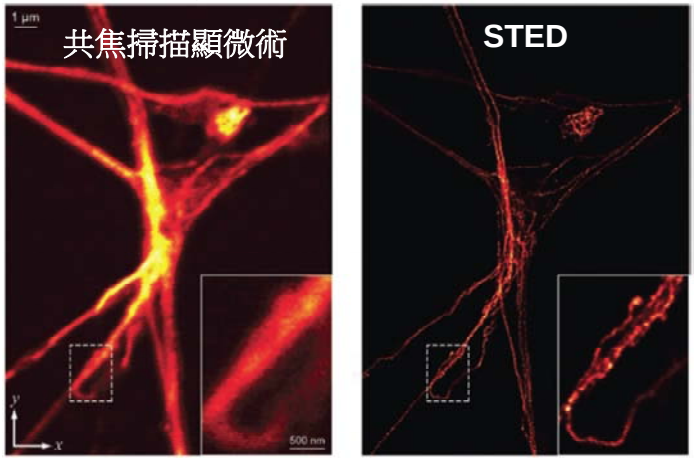
用一道像甜甜圈的雷射光，在激發光點旁邊造成受激發射耗乏，以縮小激發光點的直徑，提高橫向解析率。



大分子

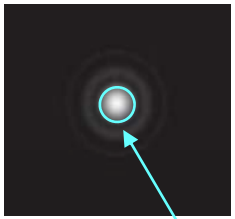


神經細胞裡的微管絲

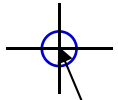


Ref: G. Donnert et al., *Proc. Natl. Acad. Sci. USA* **103,** 11440 (2006).

另一種想法：定位



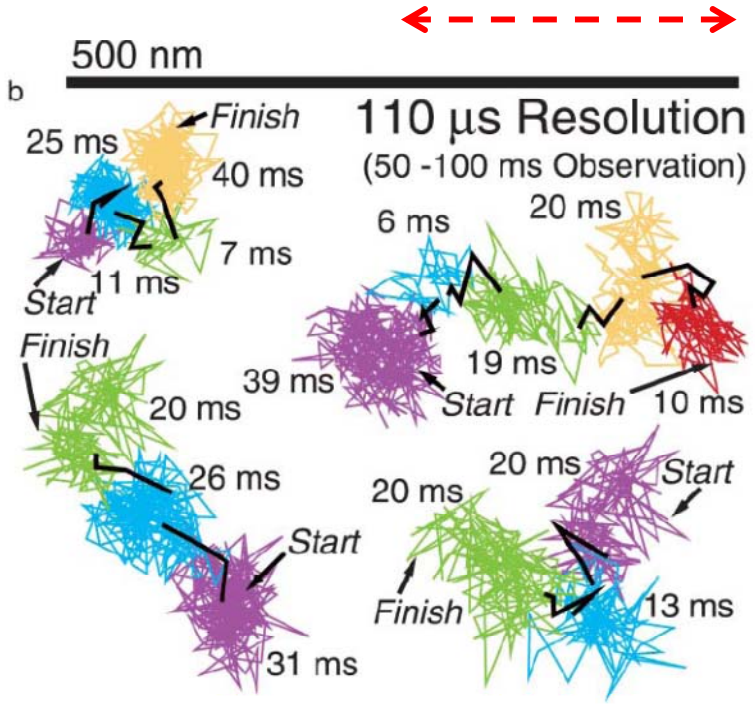
如果發光的物體夠小，我們也可以利用定位的概念，把影像一點一點組合起來。



數學上，可以利用一個二維的函數(例如一個圓盤)來表示一個小物體的影像，並且用運算的方式找出這個二維函數的中心(圓盤的圓心)。

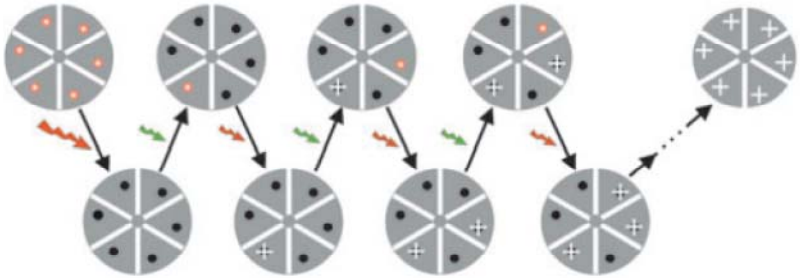
定位中心的準確度，只跟訊號的雜訊有關，跟成像的物理機制無關。因此不受到解析率極限的限制。

下圖是利用定位運算，追蹤4個40奈米金球在細胞膜上的運動軌跡。請注意尺度遠小於光學的解析率極限。

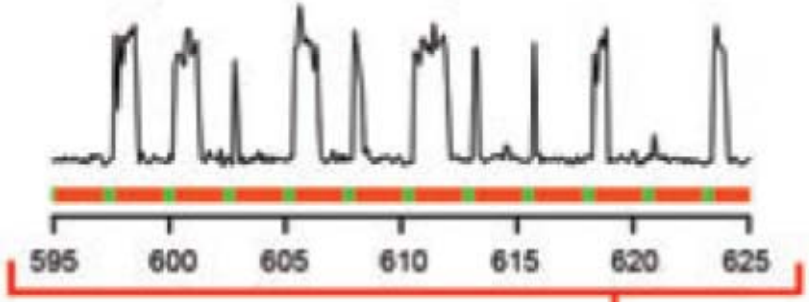


Ref: K. Murase et al., *Biophys. J.* **86,** 4075 (2004).

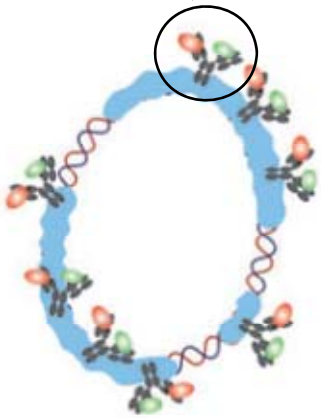
定位與光學激活的染料分子



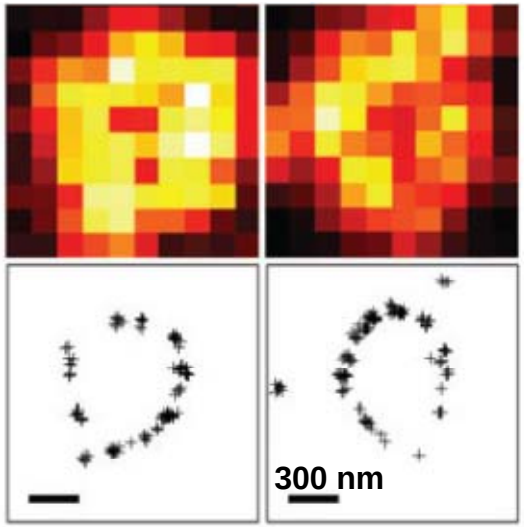
紅光是激發螢光用的，也會將染料分子打成不發光態(光漂白)。然後用綠光將部分染料分子重新活化(光激活) ，就又會發光。綠光的功率很低，因此每次照射不會將全部的染料分子都活化。而且被活化過的分子，下次就比較不容易被活化。



需要特殊設計的染料分子



傳統顯微鏡影像

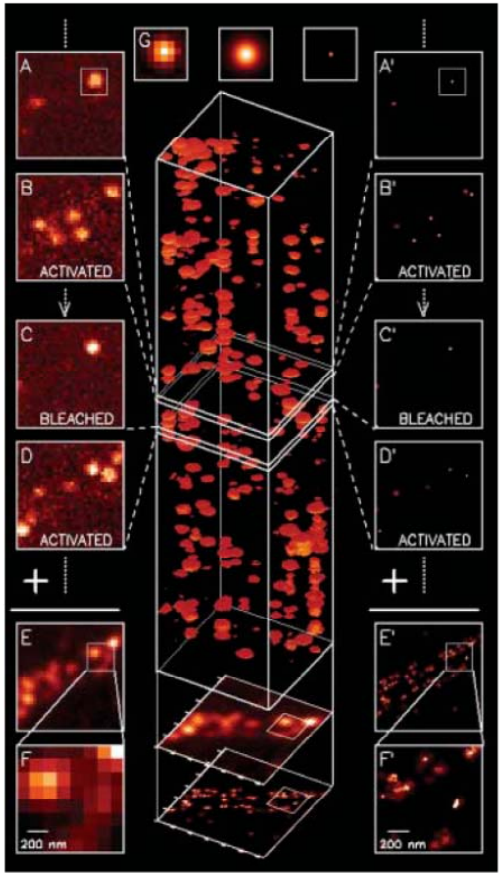


定位結果

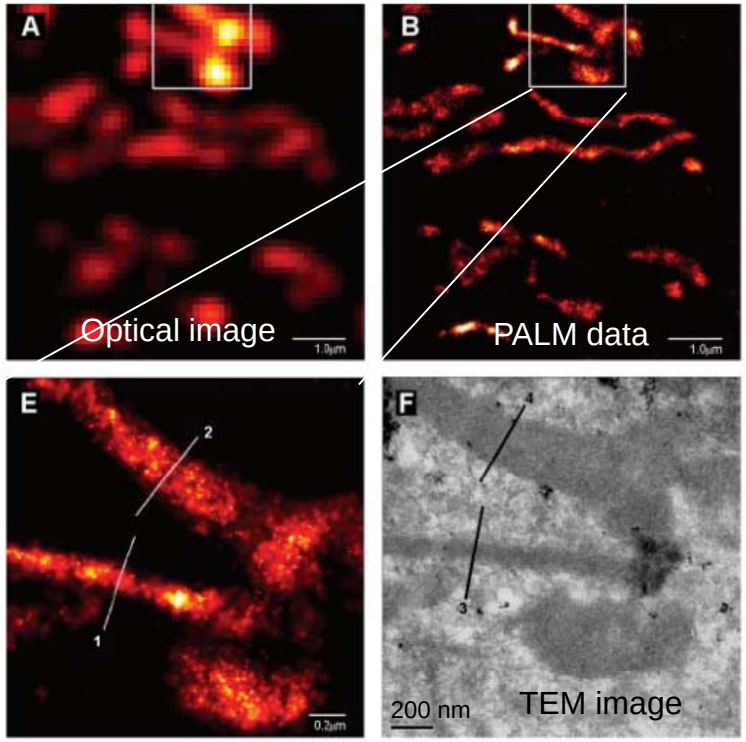
Ref: M. J. Rust, M. Bates, and X. Zhuang, *Nat. Methods* **3,** 793 (2006).

光激活定位顯微術(photo-activated localization microscopy, PALM)

傳統顯微鏡影像　　PALM



細胞中粒線體的膜蛋白(細胞色素C氧化脢)的分布

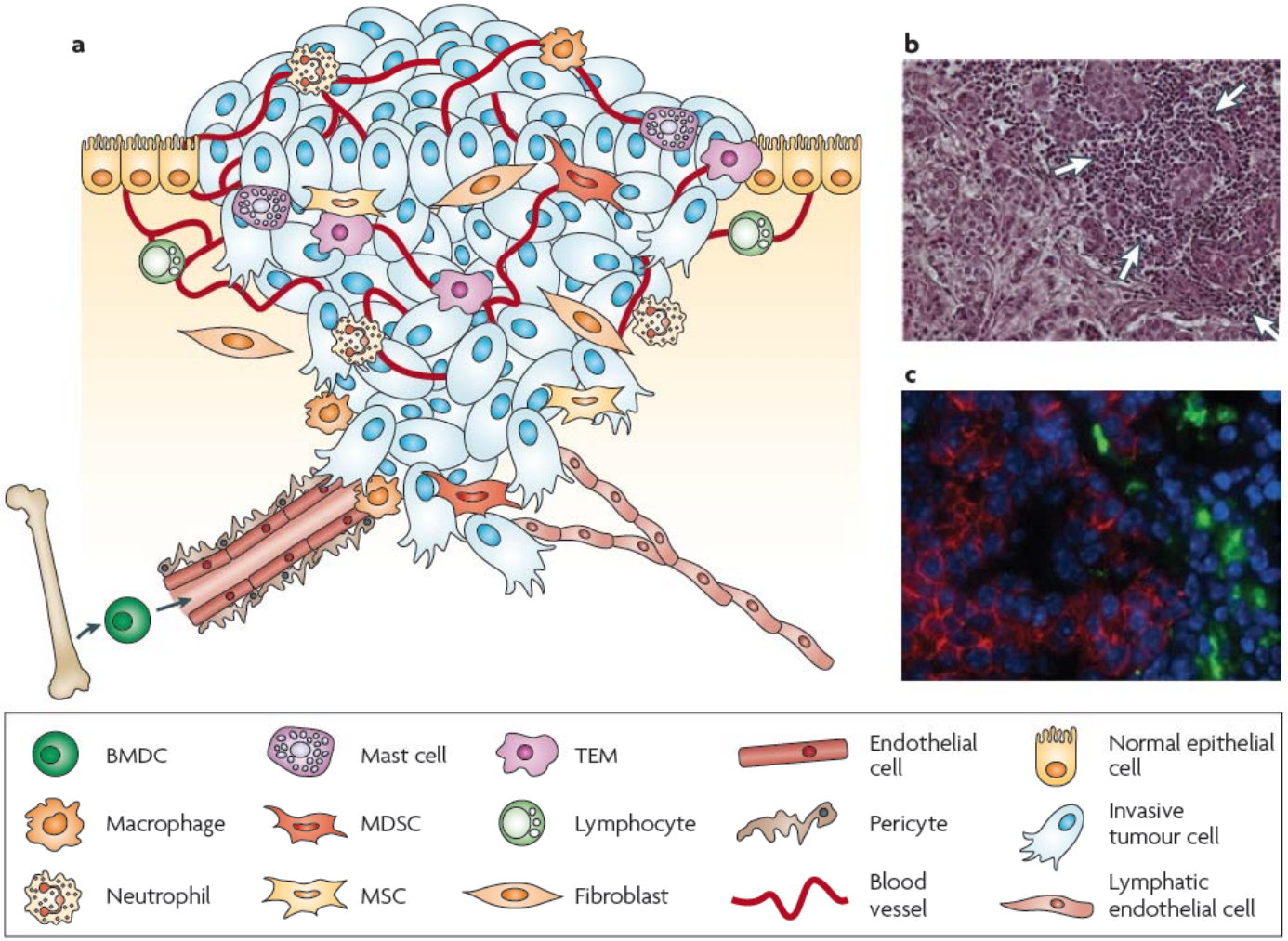


Ref: E. Betzig et al., *Science* **313,** 1642 (2006).

大綱

- 用甚麼工具看活細胞？
- 看活細胞要注意甚麼？
- 用甚麼工具能看得更清楚？
- 為什麼不能只是看一看？
- 用什麼工具可以不只是看一看？
- 物理學家要跟活細胞玩甚麼？

細胞活在很複雜的微環境裡—以癌細胞為例

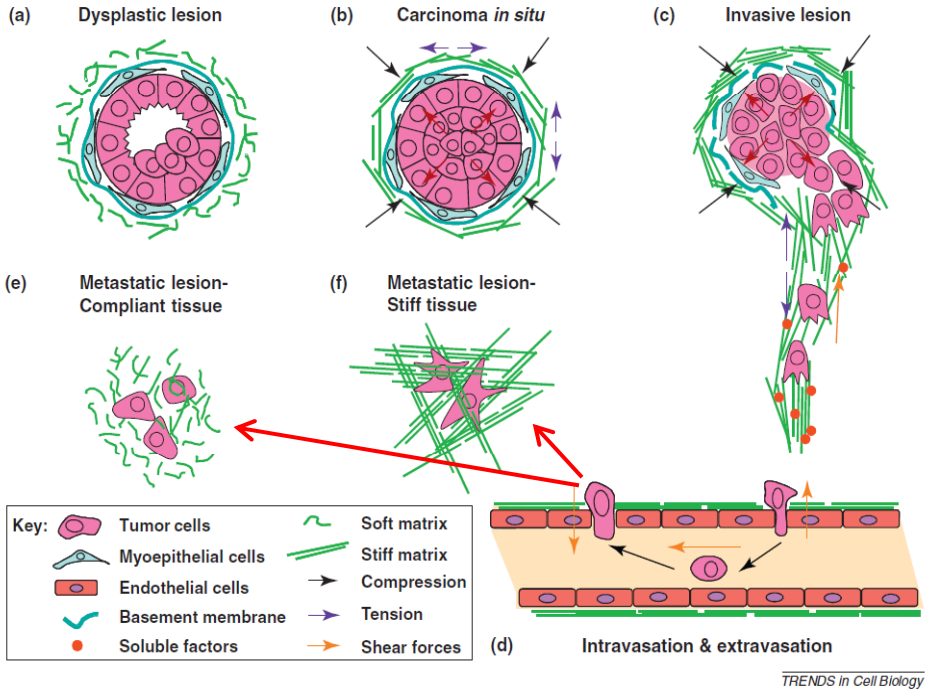


綠色是巨噬細胞
紅色是癌細胞

Ref: J. A. Joyce and J. W. Pollard, *Nat. Rev. Cancer* **9,** 239 (2009).

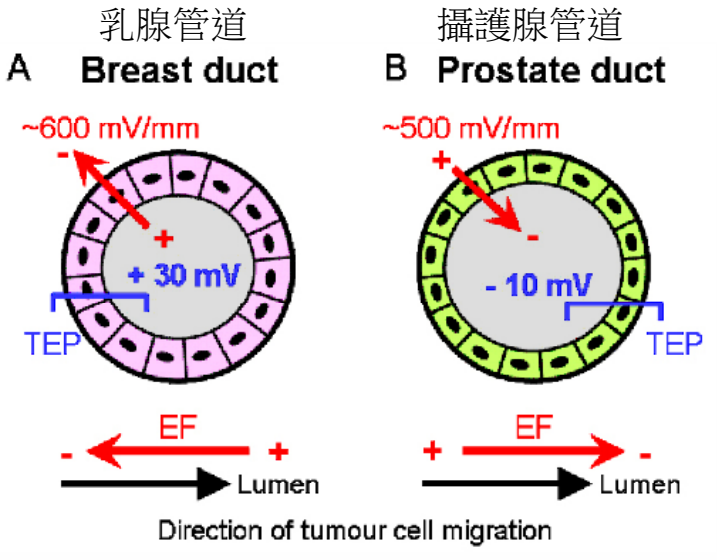
細胞的微環境裡有許多物理刺激

癌細胞進行轉移時，來自周邊組織的作用力有很大的改變



Ref: H. Yu, J. K. Mouw, and V. M. Weaver, *Trends Cell Biol.* **21,** 47 (2011).

某些組織會產生內生電場

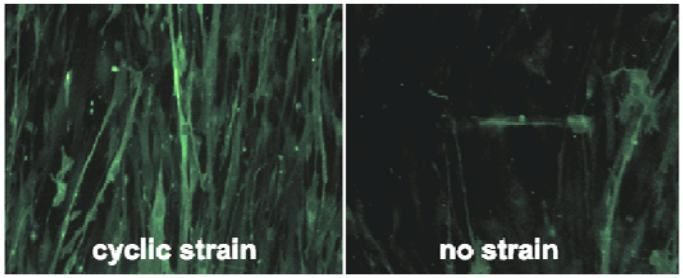


很巧的是，兩種組織的癌細胞都會朝向管道內腔移動。

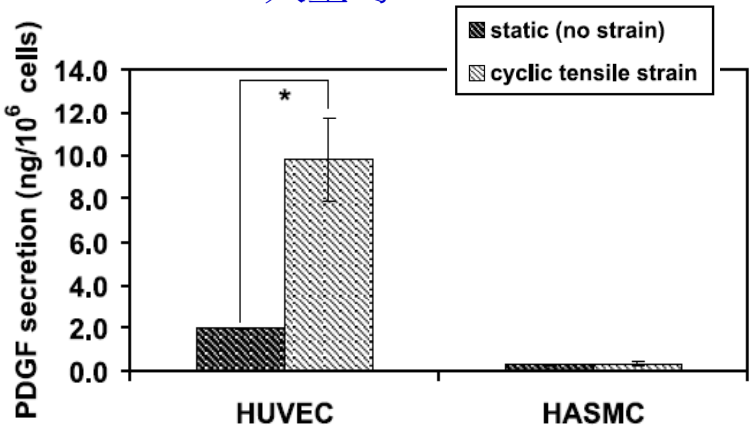
Ref: C. D. McCaig et al., *J. Cell Sci.* **122,** 4267 (2009).

物理刺激與化學刺激一起發生作用

平滑肌細胞受到週期性的拉伸，會表現大量的PDGF受體

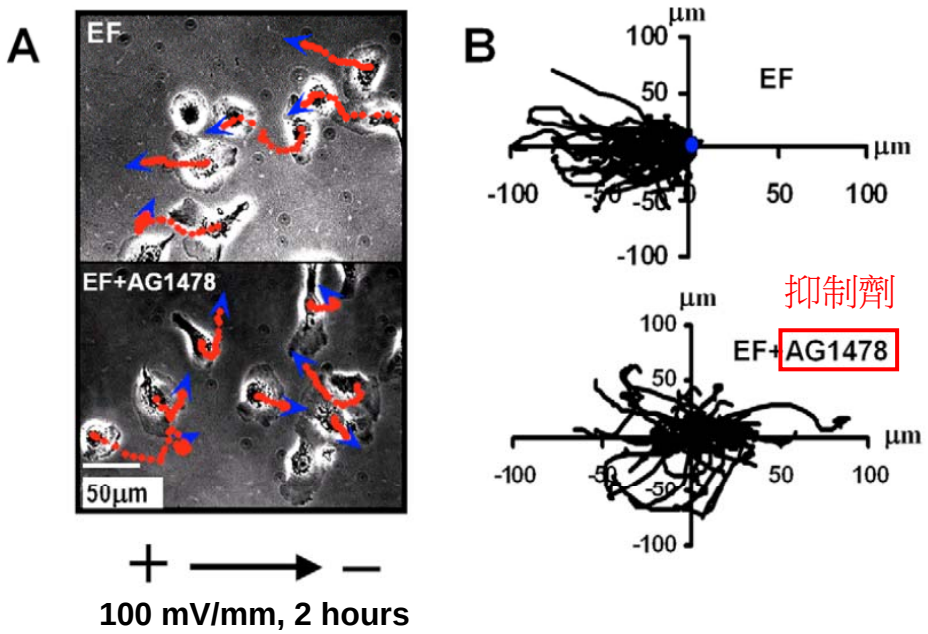


血管內皮細胞受到週期性的拉伸，會分泌大量的PDGF



Ref: Y. C. Yung et al., *Proc. Natl. Acad. Sci. U.S.A*. **106**, 15279 (2009).

乳癌細胞會往電場的正極移動



將乳癌細胞的EGF受體抑制，細胞則不會往電場的正極移動。

Ref: J. Pu et al., *J. Cell Sci.* **120,** 3395 (2007).

大綱

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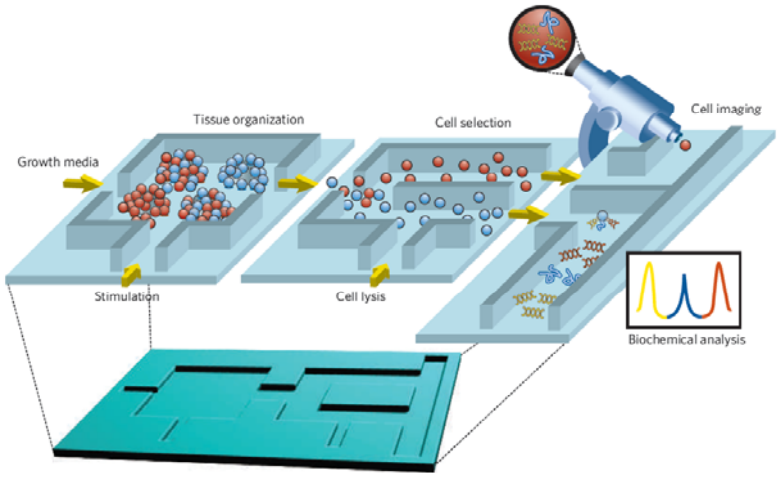
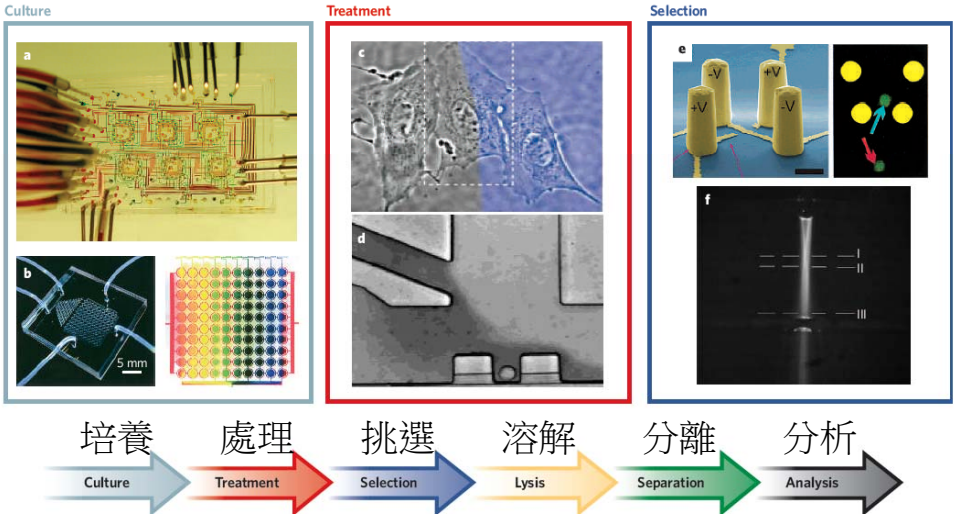
- 物理學家要跟活細胞玩甚麼？

晶（芯）片實驗室





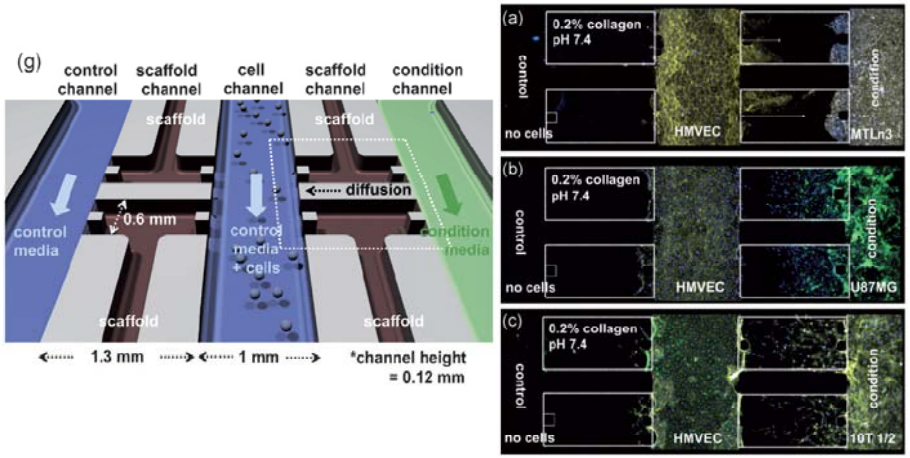
Ref: J. El-Ali et al., *Nature* **442,** 403 (2006).

優點：

- 單位培養液體積中的細胞數量約為傳統培養皿的2-3倍
- 條件化培養液可以在封閉的環境中交換
- 空間與時間參數可以精確控制
- 高解析率觀測與高靈敏度感測可以直接於晶片上執行，不需將細胞取出

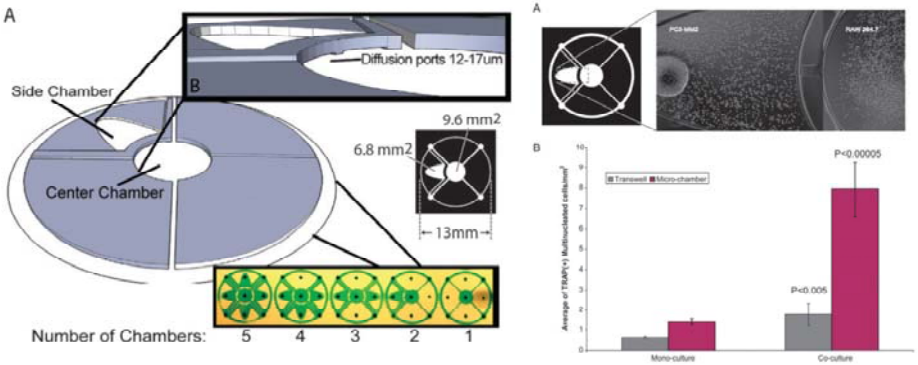
多種細胞共同培養

癌細胞、平滑肌細胞、血管內皮細胞



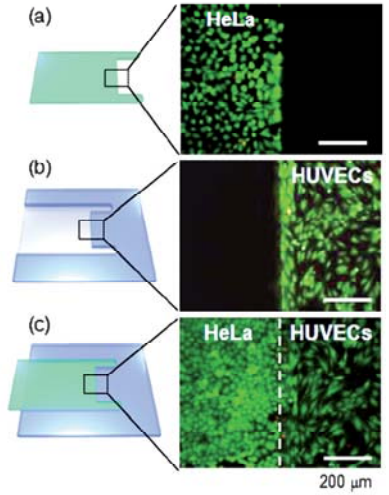
Lab Chip **9,** 269 (2009).

癌細胞、單核細胞



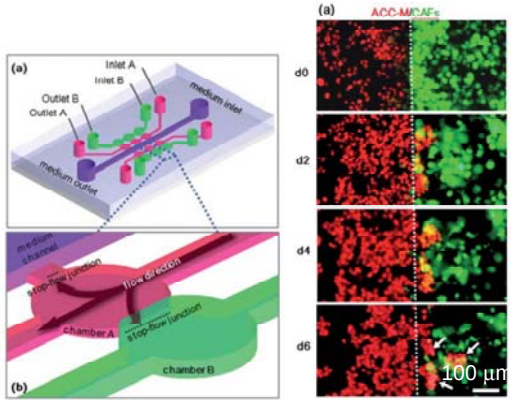
Integr. Biol. **1,** 267 (2009).

癌細胞、血管內皮細胞



Lab Chip **9,** 427 (2009).

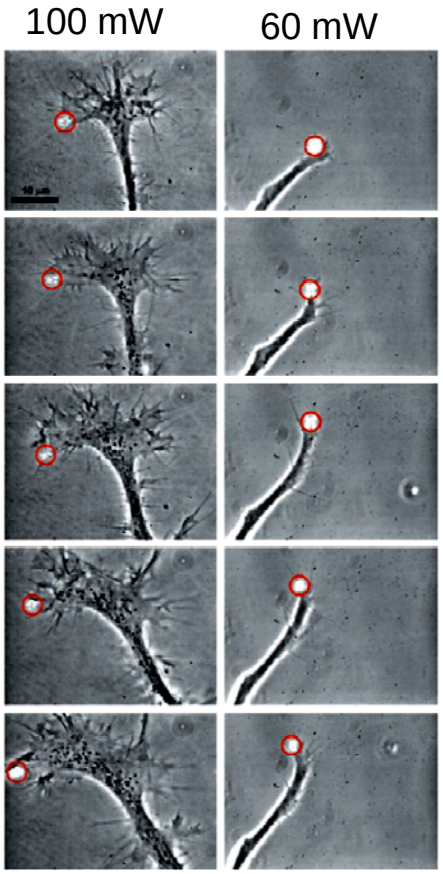
癌細胞、纖維母細胞



Lab Chip **10,** 1671 (2010).

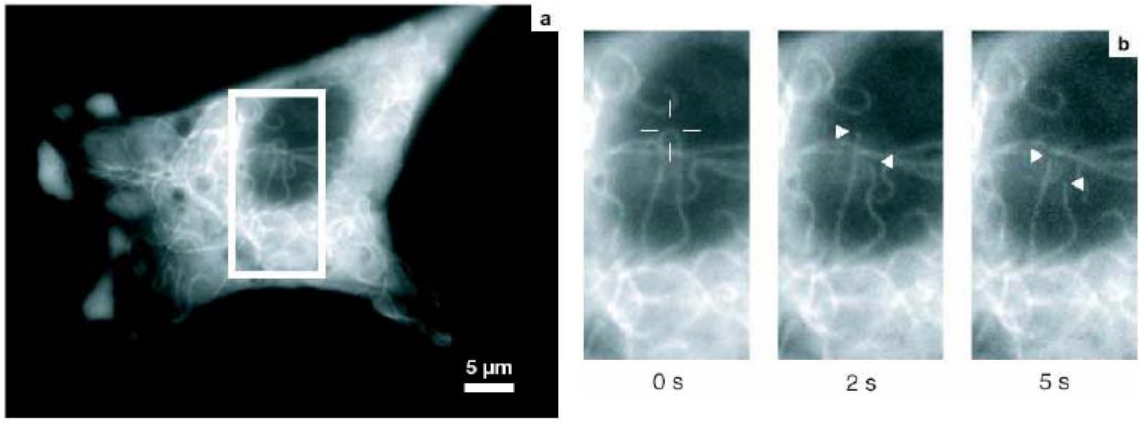
雷射光也很有用

近紅外光雷射會引導神經細胞的生長



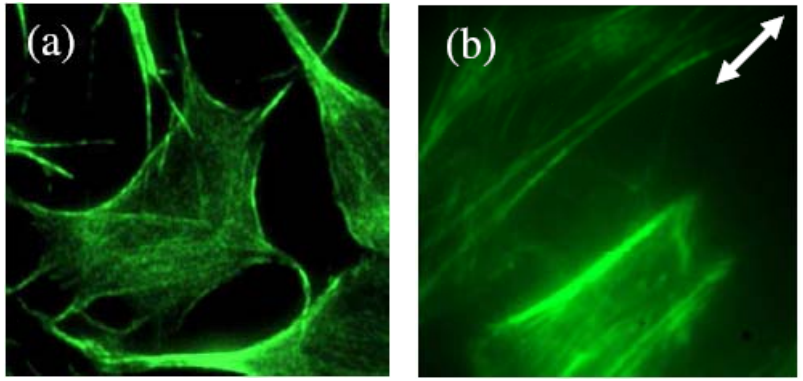
Ref: A. Ehrlicher et al., *PNAS* **99,** 16024 (2002).

飛秒(femtosecond, 10^{-15} sec)雷射脈衝可用來做細胞內手術



Ref: A. Heisterkamp et al., *Opt. Express* **13,** 3690 (2005).

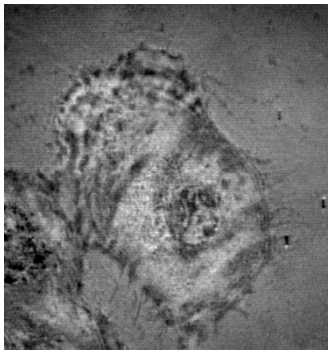
光的偏極方向可以排列細胞內的肌動蛋白微絲

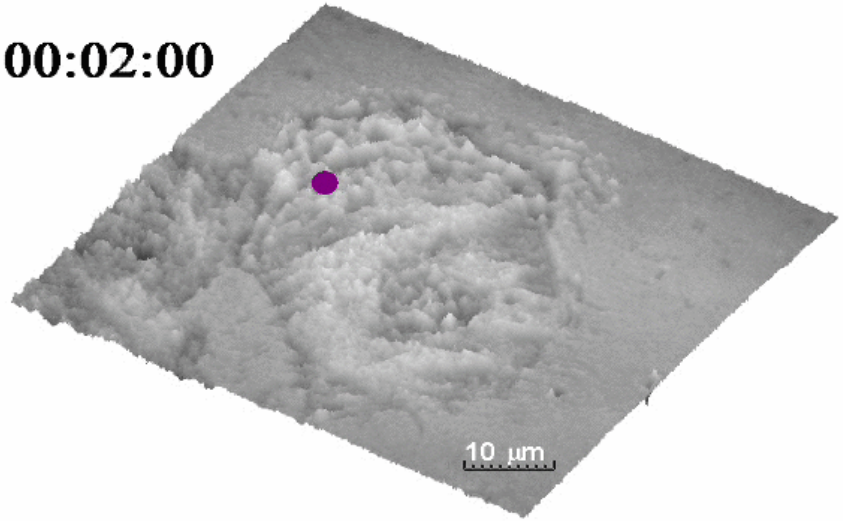


532 nm
6 mW

Ref: G. Biener et al., *Opt. Express* **17,** 9724 (2009).

細胞不喜歡紫色光(405 nm)





Laser power on the cell: 10 µW
Illumination duration: 1 sec
Illumination rate: 5 shots/min

大綱

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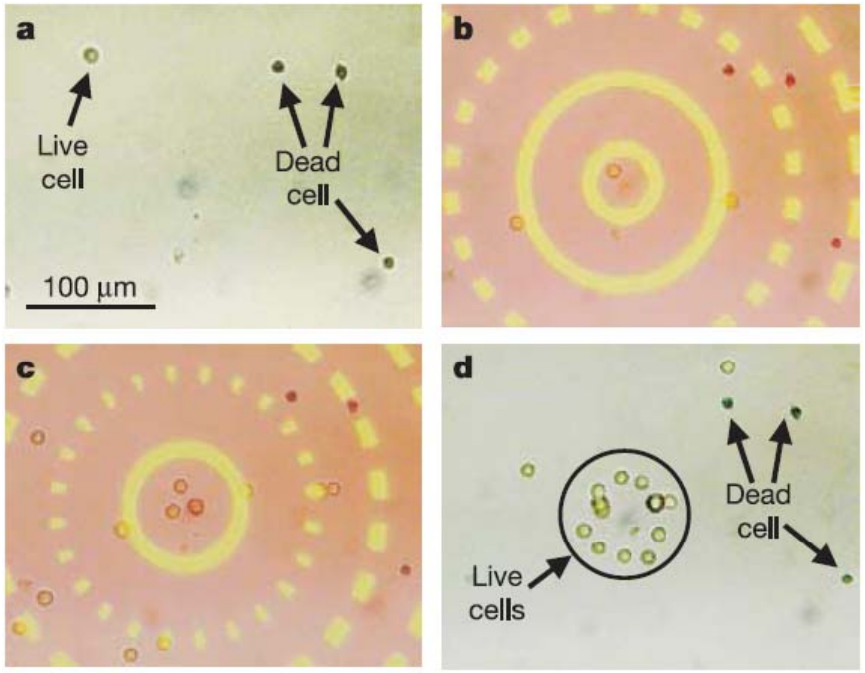
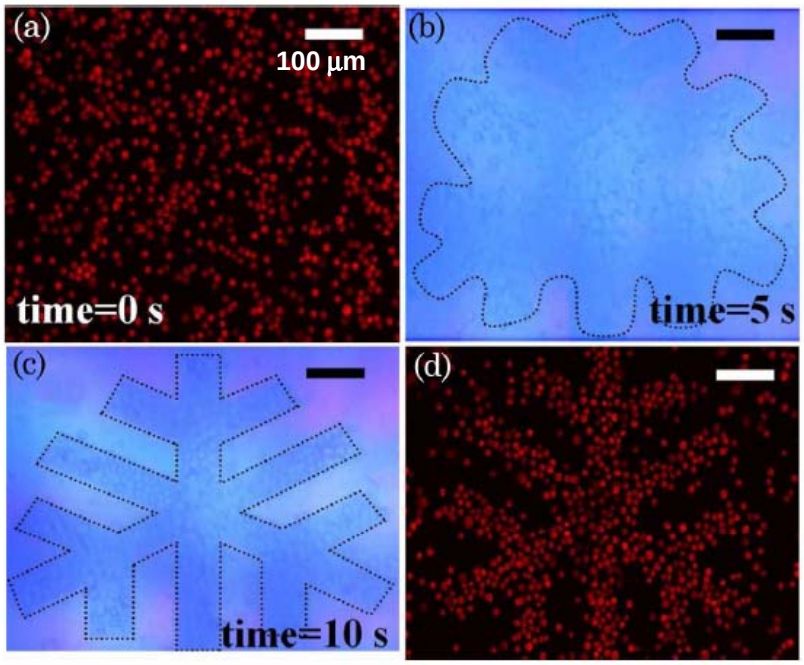
用光電效應把漂浮型細胞排列起來



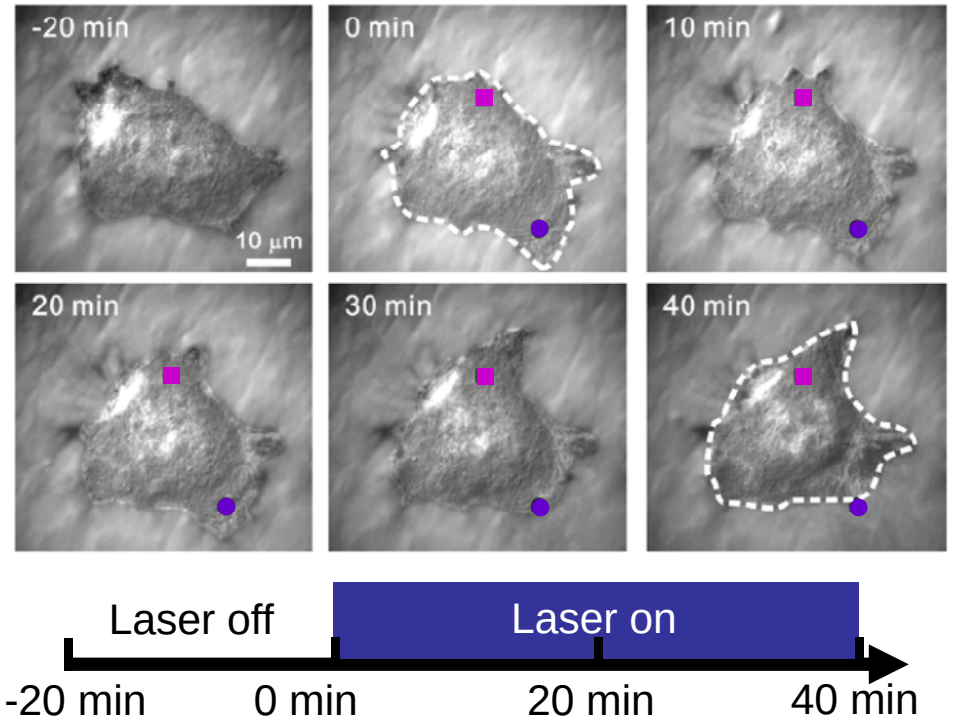
Ref: P. Y. Chiou, A. T. Ohta, and M. C. Wu, *Nature* **436,** 370 (2005).



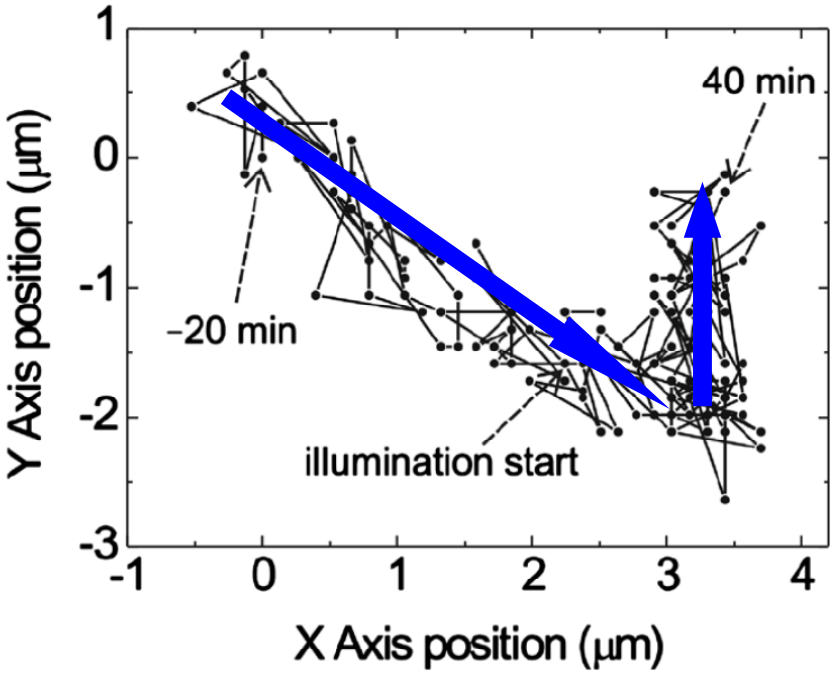
Ref: S.-M. Yang et al., *Opt. Lett.* **35,** 1959 (2010).

用不同顏色的光點改變細胞運動方向

紫色的圓點是波長405 nm的聚焦光點照射位置
粉紅色方點是波長1064 nm的聚焦光點照射位置



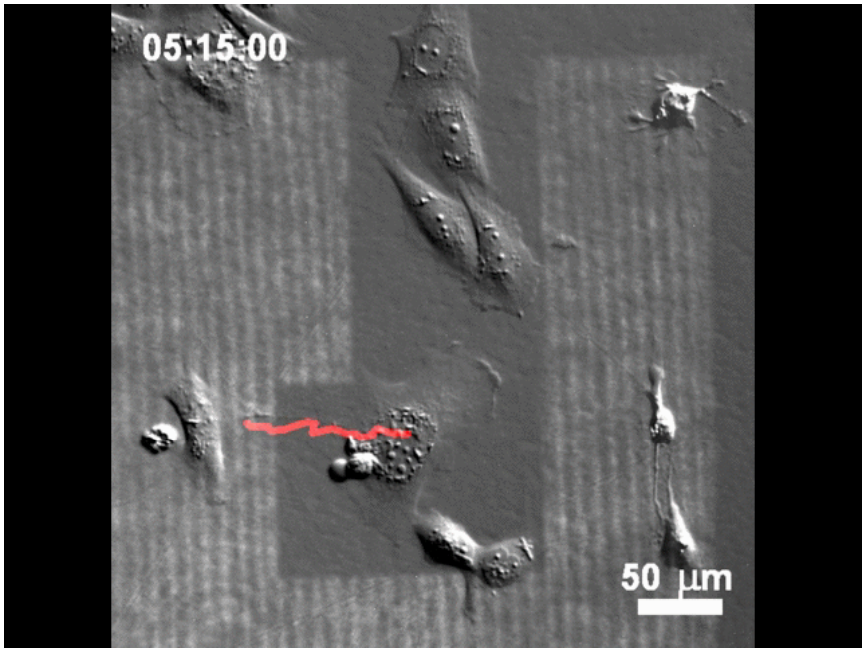
細胞中心的移動軌跡



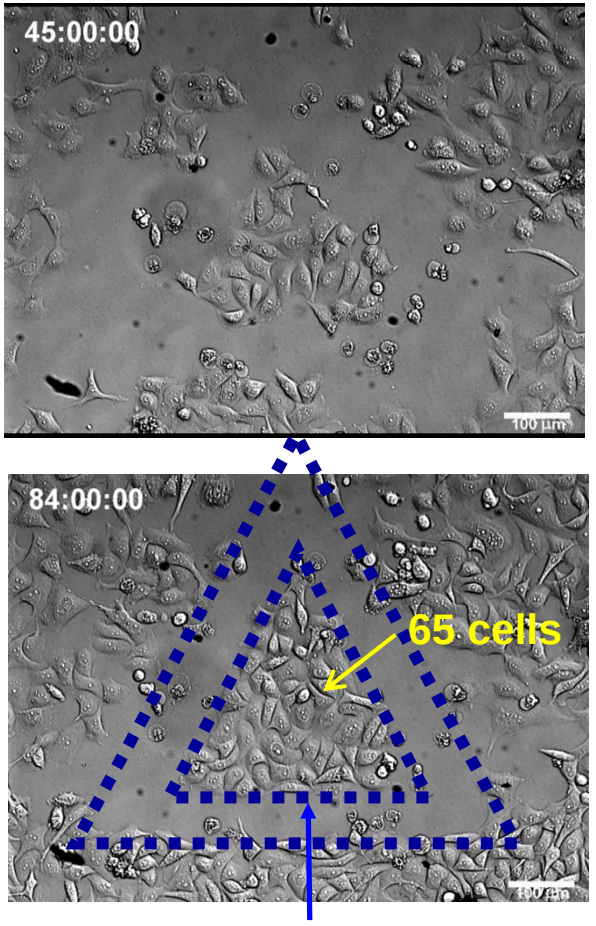
J.-L. Xiao, T.-H. Hsu, P.-Y. Hsu, W.-J. Yang, P.-L. Kuo, and C.-H. Lee, *Appl. Phys. Lett.* **97,** 203702 (2010).

用投影機產生的光圖樣控制貼附性的細胞運動

Guiding the pathway of cell migration

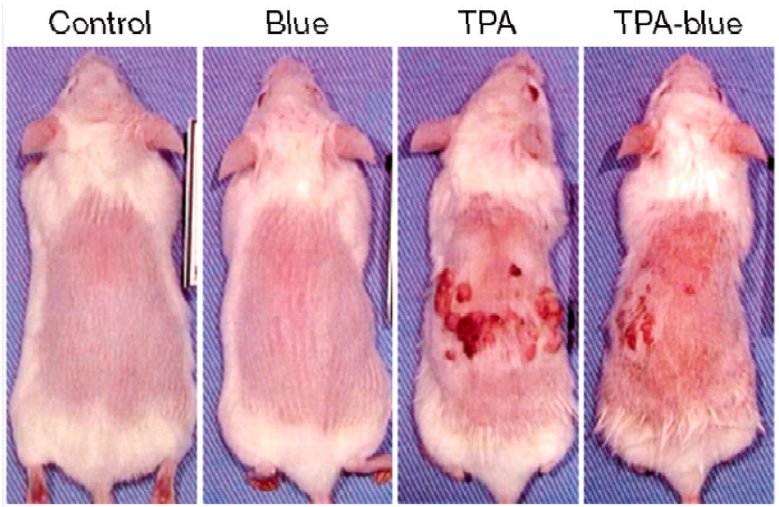


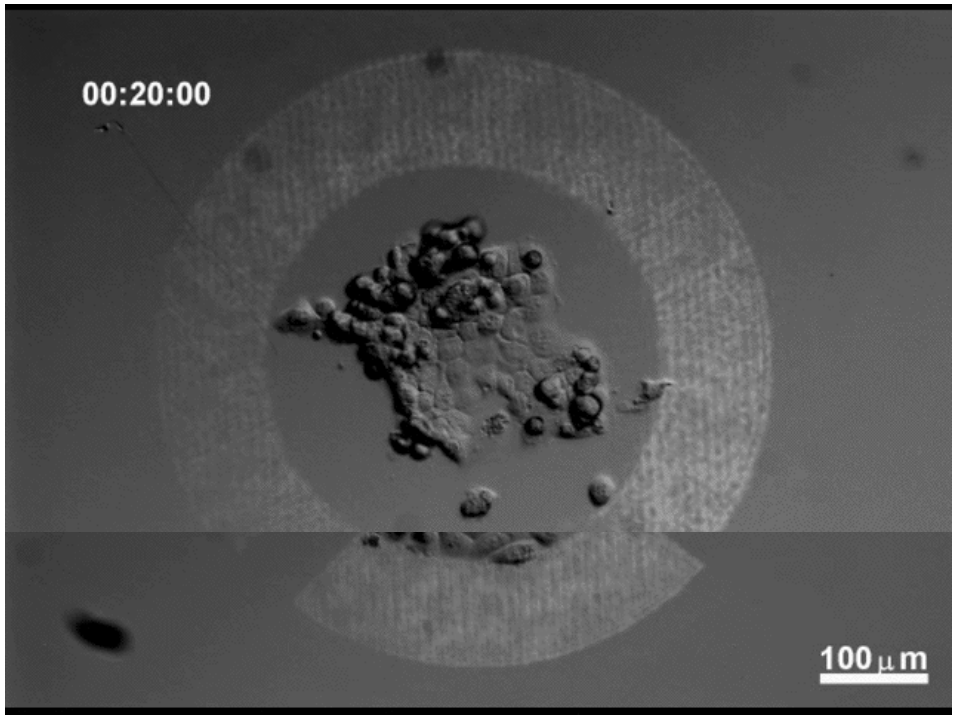
J.-L. Xiao, D.-H. Lu, and C.-H. Lee, *Appl. Phys. Lett.* **102,** 123703 (2013).



J.-L. Xiao, H.-J. Pan, and C.-H. Lee, *J. Biomed. Opt*. **17,** 075004 (2012).

藍光可以抑制某些皮膚腫瘤的生長





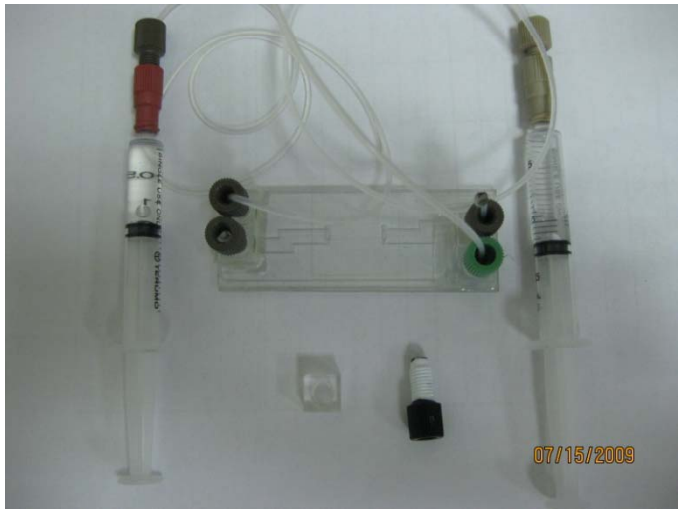
- 照射強度5.7 mW/cm^2
- 每天一小時，連續9週

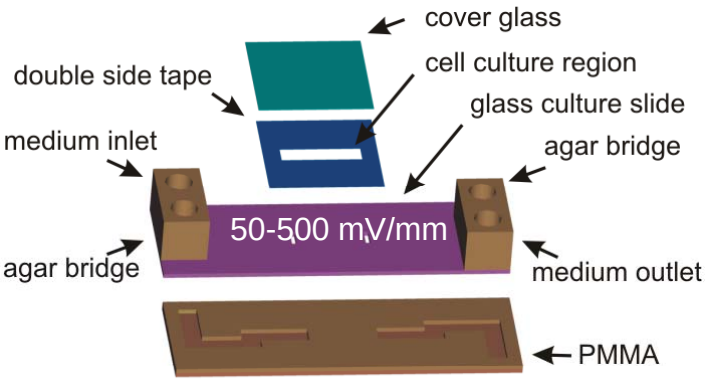
Ref: M. Ohara et al., *Cancer Sci.* **94,** 205 (2003).

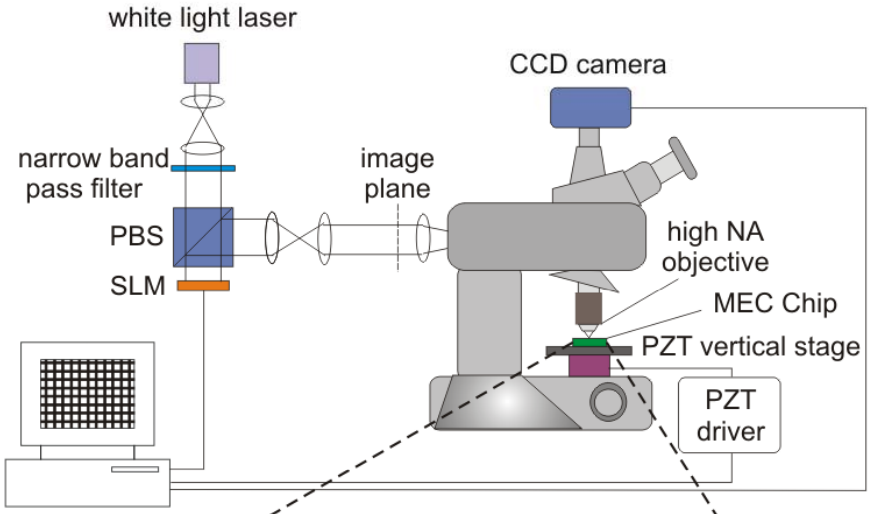
但是藍光對正常細胞也有副作用，因此不能成為一個療法。

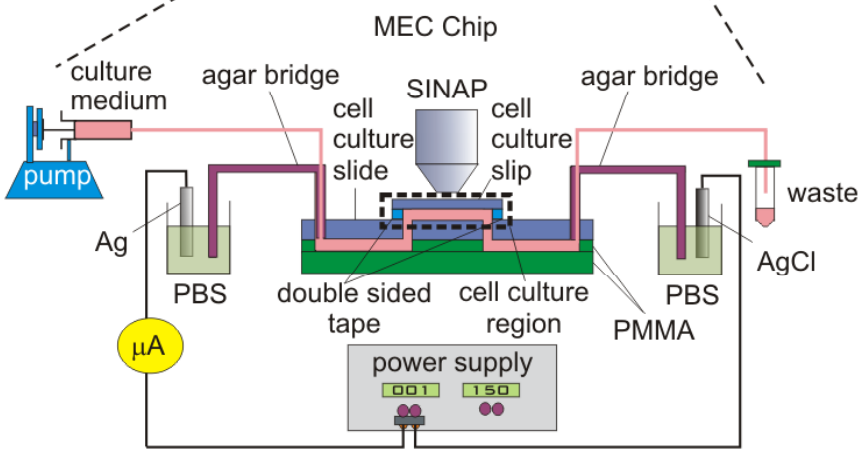
用電場芯片影響並觀察癌細胞的偽足生長情形

MEC chip



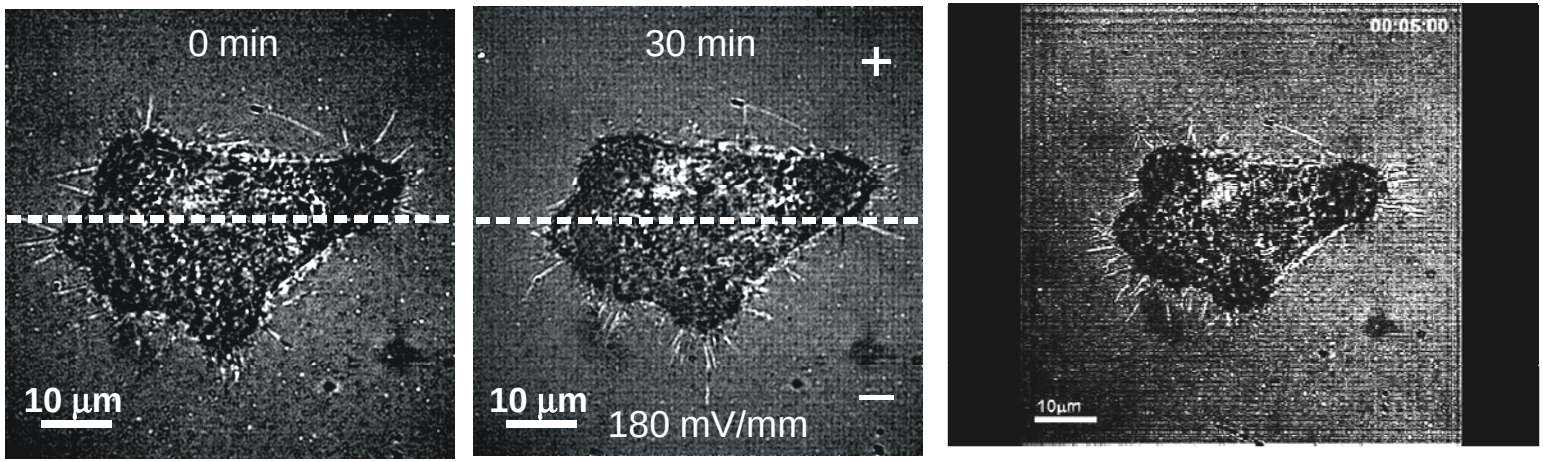




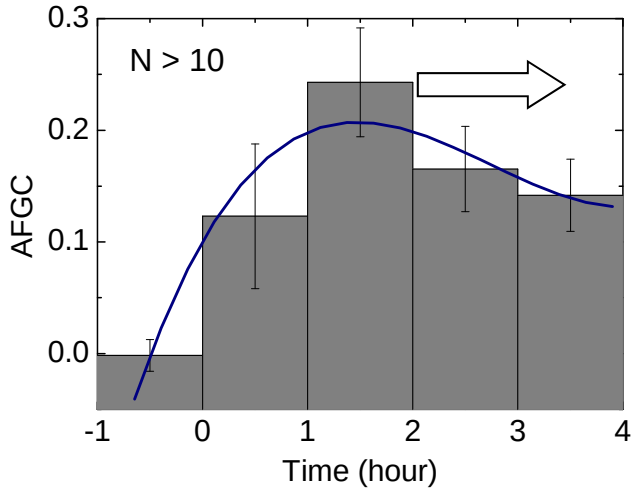


C.-W. Huang, J.-Y. Cheng, M.-H. Yen, and T.-H. Young, *Biosens. Bioelectron.* **24**, 3510 (2009).

癌細胞的絲狀偽足會朝向負極生長



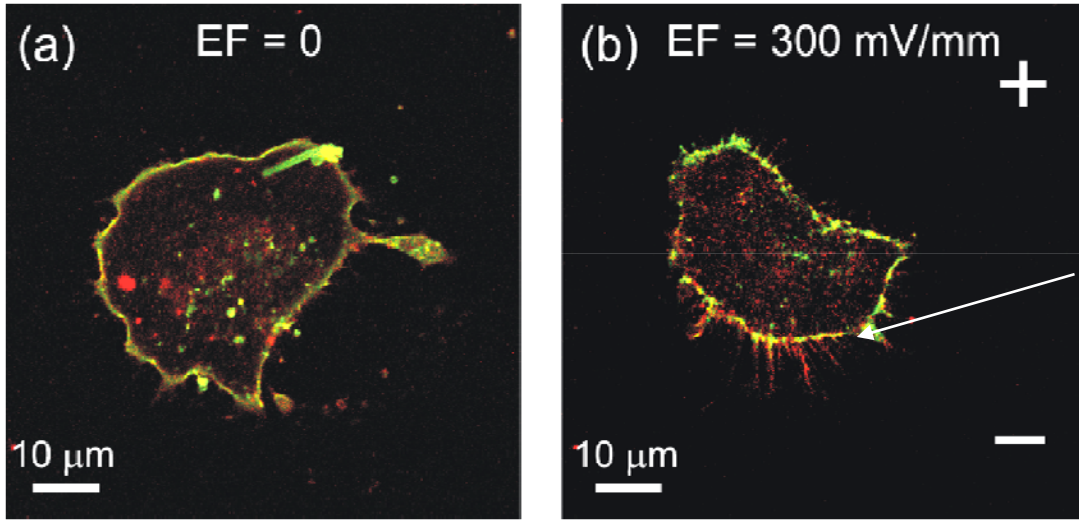
AFGC=(負極側的偽足數-正極側的偽足數)/(全部偽足數)



大約2小時後，AFGC趨向穩定

螢光顯微術可以幫忙回答一些問題

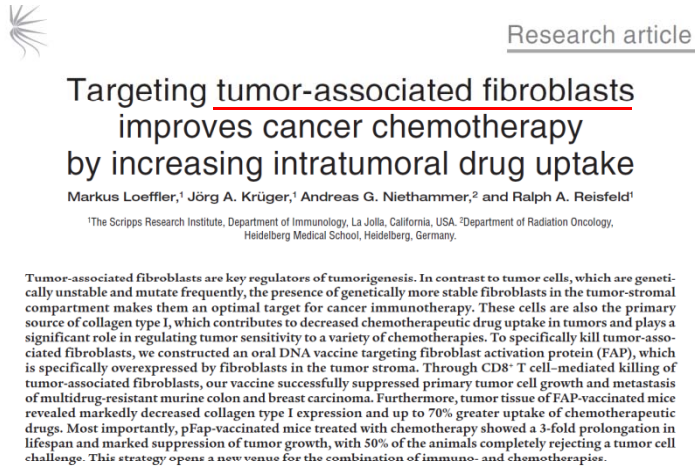
綠色：細胞膜
紅色：EGFR
黃色表示兩者在一起



EGFR會聚集在朝向負極生長的絲狀偽足裡面

C.-C. Wang, Y.-C. Kao, P.-Y. Chi, C.-W. Huang, J.-Y. Lin, C.-F. Chou, J.-Y. Cheng, and C.-H. Lee, *Lab Chip* **11,** 695 (2011).

與癌症有關的纖維母細胞(Cancer-associated fibroblast)



Research article

Targeting tumor-associated fibroblasts improves cancer chemotherapy by increasing intratumoral drug uptake

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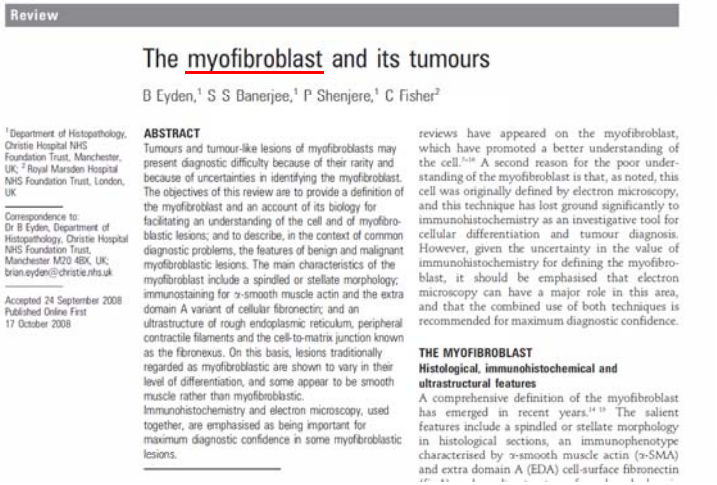
Tumor-associated fibroblasts are key regulators of tumorigenesis. In contrast to tumor cells, which are genetically unstable and mutate frequently, the presence of genetically more stable fibroblasts in the tumor-stromal compartment makes them an optimal target for cancer immunotherapy. These cells are also the primary source of collagen type I, which contributes to decreased chemotherapeutic drug uptake in tumors and plays a significant role in regulating tumor sensitivity to a variety of chemotherapies. To specifically kill tumor-associated fibroblasts, we constructed an oral DNA vaccine targeting fibroblast activation protein (FAP), which is specifically overexpressed by fibroblasts in the tumor stroma. Through $CD8^+$ T cell–mediated killing of tumor-associated fibroblasts, our vaccine successfully suppressed primary tumor cell growth and metastasis of multidrug-resistant murine colon and breast carcinoma. Furthermore, tumor tissue of FAP-vaccinated mice revealed markedly decreased collagen type I expression and up to 70% greater uptake of chemotherapeutic drugs. Most importantly, pFap-vaccinated mice treated with chemotherapy showed a 3-fold prolongation in lifespan and marked suppression of tumor growth, with 50% of the animals completely rejecting a tumor cell challenge. This strategy opens a new venue for the combination of immuno- and chemotherapies.

J. Clin. Invest., 2006.



Review

The myofibroblast and its tumours

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ABSTRACT

Tumours and tumour-like lesions of myofibroblasts may present diagnostic difficulty because of their rarity and because of uncertainties in identifying the myofibroblast. The objectives of this review are to provide a definition of the myofibroblast and an account of its biology for facilitating an understanding of the cell and of myofibroblastic lesions; and to describe, in the context of common diagnostic problems, the features of benign and malignant myofibroblastic lesions. The main characteristics of the myofibroblast include a spindled or stellate morphology; immunostaining for α-smooth muscle actin and the extra domain A variant of cellular fibronectin; and an ultrastructure of rough endoplasmic reticulum, peripheral contractile filaments and the cell-to-matrix junction known as the fibronexus. On this basis, lesions traditionally regarded as myofibroblastic are shown to vary in their level of differentiation, and some appear to be smooth muscle rather than myofibroblastic. Immunohistochemistry and electron microscopy, used together, are emphasised as being important for maximum diagnostic confidence in some myofibroblastic lesions.

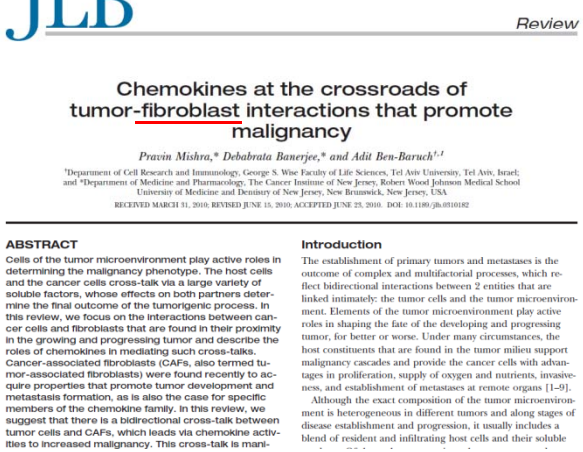
reviews have appeared on the myofibroblast, which have promoted a better understanding of the cell.[3–16] A second reason for the poor understanding of the myofibroblast is that, as noted, this cell was originally defined by electron microscopy, and this technique has lost ground significantly to immunohistochemistry as an investigative tool for cellular differentiation and tumour diagnosis. However, given the uncertainty in the value of immunohistochemistry for defining the myofibroblast, it should be emphasised that electron microscopy can have a major role in this area, and that the combined use of both techniques is recommended for maximum diagnostic confidence.

THE MYOFIBROBLAST

Histological, immunohistochemical and ultrastructural features

A comprehensive definition of the myofibroblast has emerged in recent years.[14 15] The salient features include a spindled or stellate morphology in histological sections, an immunophenotype characterised by α-smooth muscle actin (α-SMA) and extra domain A (EDA) cell-surface fibronectin

J. Clin. Pathol., 2009.



JLB Review

Chemokines at the crossroads of tumor-fibroblast interactions that promote malignancy

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ABSTRACT

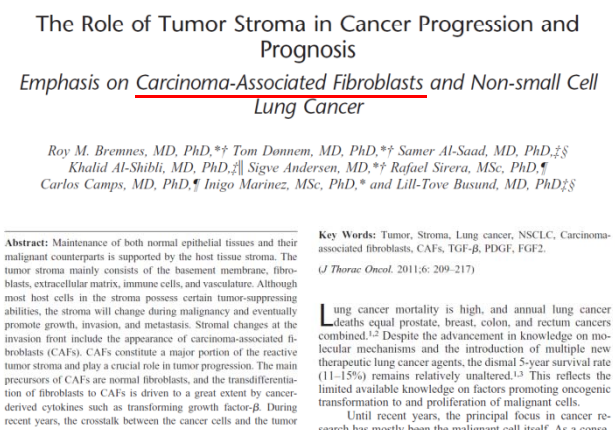
Cells of the tumor microenvironment play active roles in determining the malignancy phenotype. The host cells and the cancer cells cross-talk via a large variety of soluble factors, whose effects on both partners determine the final outcome of the tumorigenic process. In this review, we focus on the interactions between cancer cells and fibroblasts that are found in their proximity in the growing and progressing tumor and describe the roles of chemokines in mediating such cross-talks. Cancer-associated fibroblasts (CAFs, also termed tumor-associated fibroblasts) were found recently to acquire properties that promote tumor development and metastasis formation, as is also the case for specific members of the chemokine family. In this review, we suggest that there is a bidirectional cross-talk between tumor cells and CAFs, which leads via chemokine activities to increased malignancy. This cross-talk is mani-

Introduction

The establishment of primary tumors and metastases is the outcome of complex and multifactorial processes, which reflect bidirectional interactions between 2 entities that are linked intimately: the tumor cells and the tumor microenvironment. Elements of the tumor microenvironment play active roles in shaping the fate of the developing and progressing tumor, for better or worse. Under many circumstances, the host constituents that are found in the tumor milieu support malignancy cascades and provide the cancer cells with advantages in proliferation, supply of oxygen and nutrients, invasiveness, and establishment of metastases at remote organs [1–9].

Although the exact composition of the tumor microenvironment is heterogeneous in different tumors and along stages of disease establishment and progression, it usually includes a blend of resident and infiltrating host cells and their soluble

J. Leuk. Biol., 2011.



State of the Art: Concise Review

The Role of Tumor Stroma in Cancer Progression and Prognosis

Emphasis on Carcinoma-Associated Fibroblasts and Non-small Cell Lung Cancer

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Abstract: Maintenance of both normal epithelial tissues and their malignant counterparts is supported by the host tissue stroma. The tumor stroma mainly consists of the basement membrane, fibroblasts, extracellular matrix, immune cells, and vasculature. Although most host cells in the stroma possess certain tumor-suppressing abilities, the stroma will change during malignancy and eventually promote growth, invasion, and metastasis. Stromal changes at the invasion front include the appearance of carcinoma-associated fibroblasts (CAFs). CAFs constitute a major portion of the reactive tumor stroma and play a crucial role in tumor progression. The main precursors of CAFs are normal fibroblasts, and the transdifferentiation of fibroblasts to CAFs is driven to a great extent by cancer-derived cytokines such as transforming growth factor-β. During recent years, the crosstalk between the cancer cells and the tumor

Key Words: Tumor, Stroma, Lung cancer, NSCLC, Carcinoma-associated fibroblasts, CAFs, TGF-β, PDGF, FGF2.

(*J Thorac Oncol.* 2011;6: 209–217)

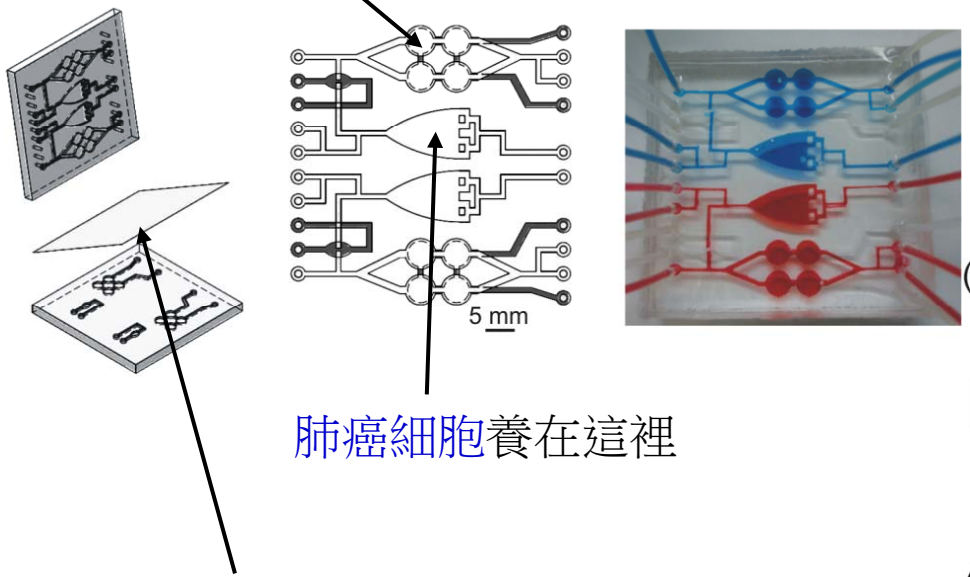
Lung cancer mortality is high, and annual lung cancer deaths equal prostate, breast, colon, and rectum cancers combined.[1,2] Despite the advancement in knowledge on molecular mechanisms and the introduction of multiple new therapeutic lung cancer agents, the dismal 5-year survival rate (11–15%) remains relatively unaltered.[1,3] This reflects the limited available knowledge on factors promoting oncogenic transformation to and proliferation of malignant cells.

Until recent years, the principal focus in cancer re-

J. Thorac. Oncol., 2011.

探討週期性拉伸對纖維母細胞的影響

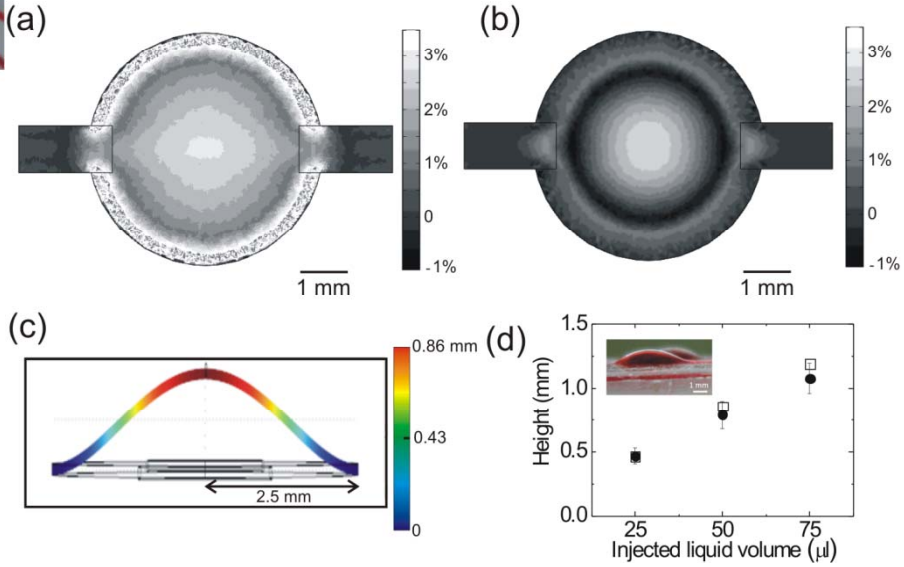
肺纖維母細胞養在這裡，其下方有液壓腔



肺癌細胞養在這裡

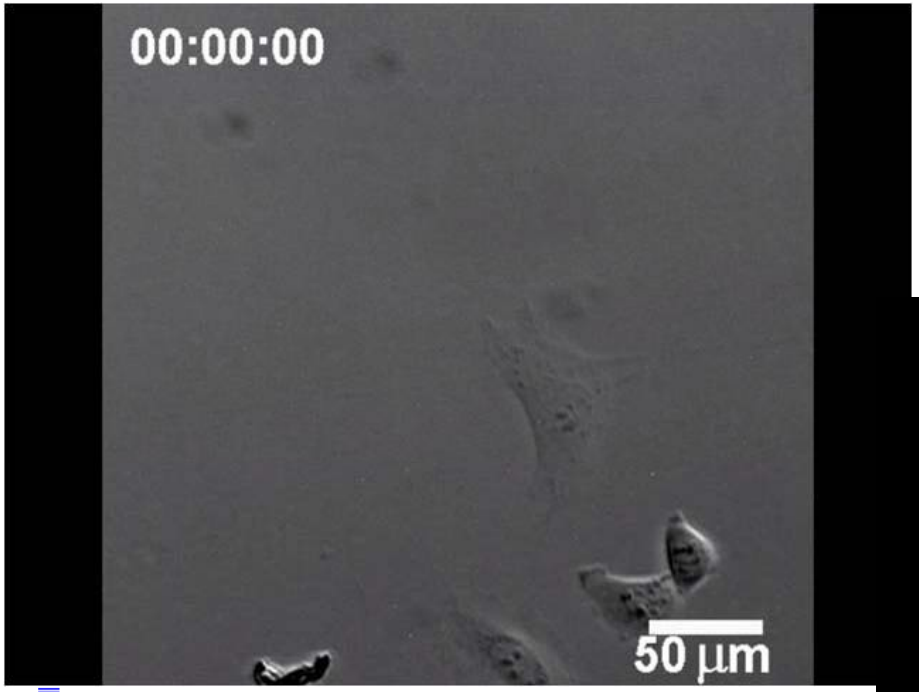
中間的塑膠膜只有0.1 mm厚，因此可以被灌注到下方空腔的液體推動，發生形變。我們將形變的頻率設定為正常呼吸的頻率(0.27 Hz)。

利用電腦模擬計算出切線方向(a)與半徑方向(b)的形變量($\Delta x/x_0$)，在中心部分都超過3%

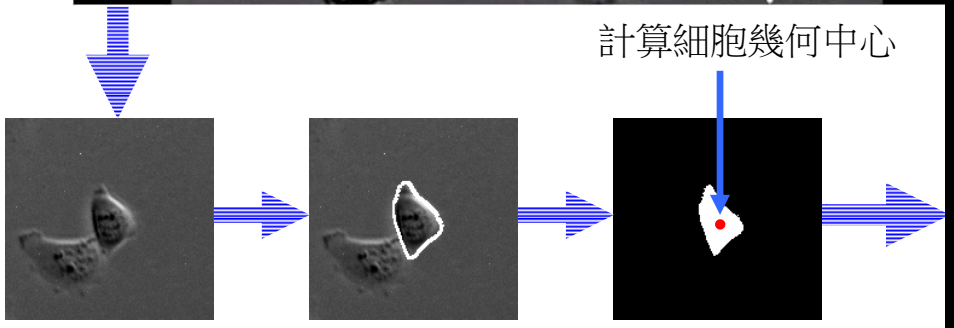


灌注液體到下方空腔後，測量中間的塑膠膜被頂高的程度，與電腦模擬的結果(c)比較。

紀錄不同條件下的癌細胞移動速率

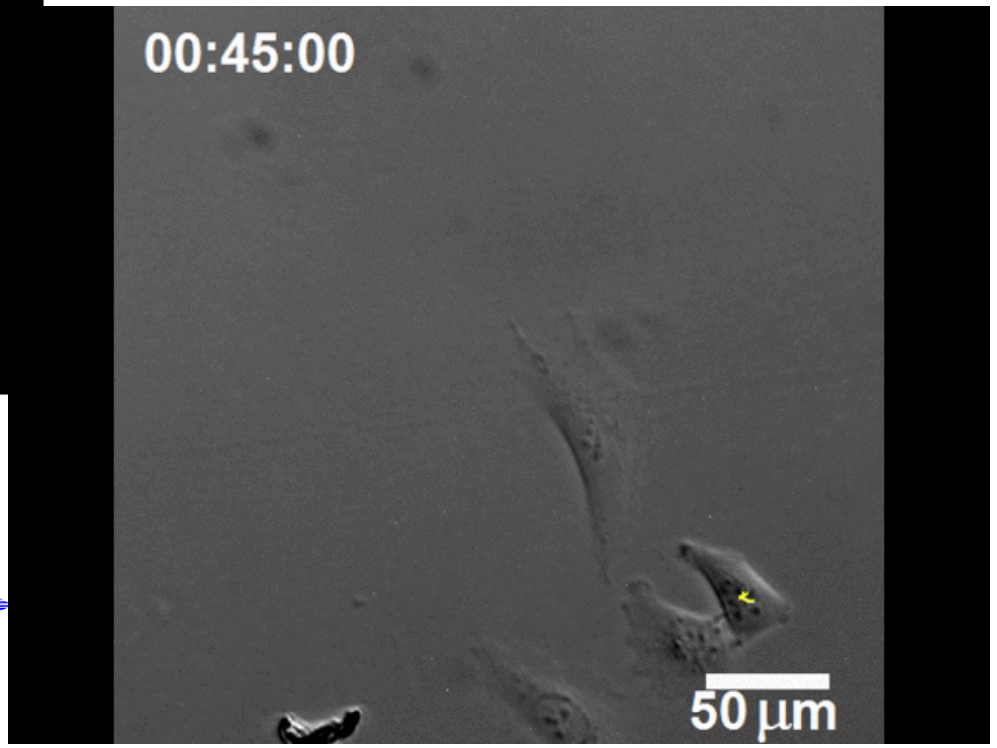


計算細胞幾何中心

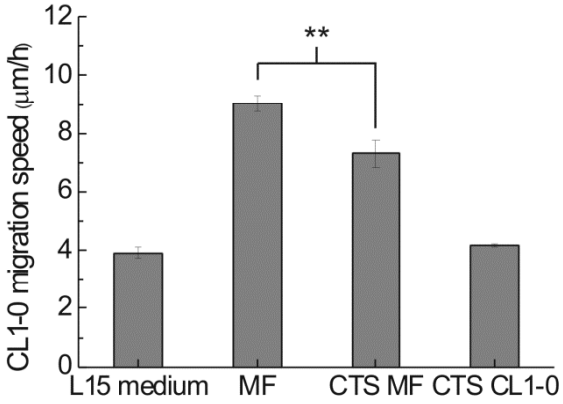


標出細胞邊緣

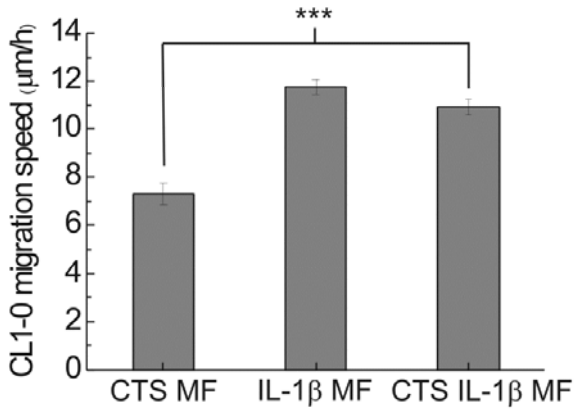
由細胞運動路徑長度與時間算出平均速率



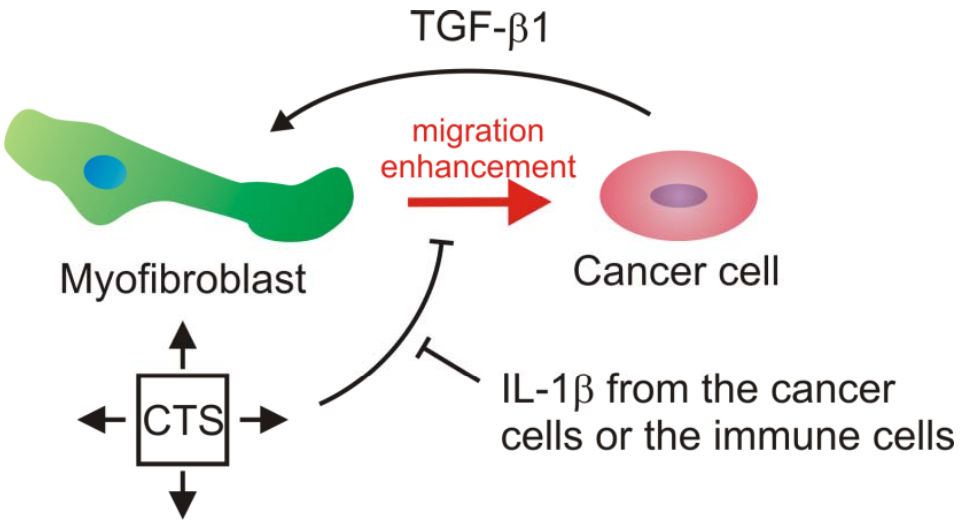
纖維母細胞會提高癌細胞移動速率，但週期性拉伸會降低這個能力



週期性拉伸會降低纖維母細胞提高肺癌細胞移動速率的能力。



發炎因子IL-1β會抵消週期性拉伸對纖維母細胞的影響。



作用在纖維母細胞上的週期性拉伸會降低纖維母細胞提高肺癌細胞移動速率的能力，可能有助於防止癌細胞轉移。不過，如果腫瘤周邊有發炎反應，則週期性拉伸的功效會被抵消。

J.-W. Huang et al., *Lab Chip* **13,** 1114 (2013).

可以想一想

- 一種工具不夠
- 一個人的知識不夠
- 如何讓更多物理科學家幫忙細胞研究？
- 如何讓更多細胞生物學家想要跟物理學家合作？
- 有甚麼新價值？

諾貝爾物理獎得主，也做細胞研究

Meeting Home
Abstracts/Posters (+)
Fees and Deadlines
Submission Guidelines
Submission Instructions
Editing and Withdrawing
Publication and Citation
Abstract/Poster FAQs
Oral Presentation
Poster Guidelines
Minisymp/Poster Topics
Poster Guidelines
Program
Career
Moscone Center
San Francisco (+)
Restaurant Listings
Reservations Tonight!
Local Area Information
Exhibits
General Information (+)
Meeting Overview
Attendee FAQs
Disabilities/Special Needs
Children
Meeting Policies
Volunteer Opportunities
Graduate School Fair
Hotel and Travel (+)
Hotel List
Reserve a Room
Transportation/Parking

2012 ASCB Annual Meeting (美國細胞生物學會年會)

Cell Biology and the Physical Sciences Thread

Keynote Speaker: Steven Chu, U.S. Secretary of Energy

No one would dispute that living organisms must operate within the confines of the basic laws of physics and chemistry, and the thinking and methodologies of the physical sciences play an increasingly important role in understanding biological systems. We are entering an era in which more physical scientists are attracted to problems of biology, and biologists seek to use tools and thinking from computation, physics, chemistry, and engineering. We hope to attract physical and computational scientists to the meeting by providing them with numerous specially designed sessions (see below) through the Cell Biology and Physical Sciences Thread. For the core cell biology community, we are introducing a Frontier Symposium, Minisymposia, and poster sessions (see below) that will address topics of how the physical and computational sciences are being applied in biology. These will enable both junior and senior scientists to learn and think of new strategies that might pertain to their work. We will also have informal discussion tables and social activities that will serve to network scientists undertaking cell biology and physical science approaches

Saturday

- Workshop: Open Problems in Biology Requiring the Physical Sciences, organized by *Julie Theriot*, *Rob Phillips*, and *Dan Fletcher*
- Special Interest Subgroups
- Meet and Greet: All are welcome, especially those attending from the physical sciences and biotech fields or others who are coming to the ASCB meeting for the first time.
- Keynote Speaker: *Steven Chu*, U.S. Secretary of Energy (*public invited via online registration*)

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