Kinetics of Molecular Binding to Surfaces and Patterning

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Lecture: 2/7

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Outline

A common way to chemically modify a surface is to expose it to molecules in solution and let the chemistry do the job.

But how long time will it take to modify the surface? It could depend on:

- Concentration of the molecules in solution.
- Diffusion constant of the molecules.
- Flow of the liquid.

We will also look at how patterns of molecules can be created on surfaces.

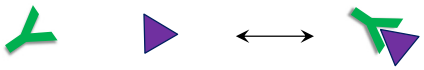
Rate Constants

Assume we have a chemical reaction where two molecules bind reversibly:

A + B ↔ AB

Recall the *law of mass action* which says the rate is proportional to the concentrations of the species that need to meet.

Rate of association: $k_{on}C_AC_B$



Rate of dissociation: $k_{off}C_{AB}$

Changes in amount of AB with time: $\frac{\partial C_{AB}}{\partial t} = k_{on}C_AC_B - k_{off}C_{AB}$

At equilibrium the rates are equal: $k_{on}\{C_AC_B\}_{t\to\infty} = k_{off}\{C_{AB}\}_{t\to\infty}$

The *dissociation constant* (unit of concentration) is: $K_D = \frac{k_{off}}{k_{on}} = \left\{\frac{C_AC_B}{C_{AB}}\right\}_{t\to\infty}$

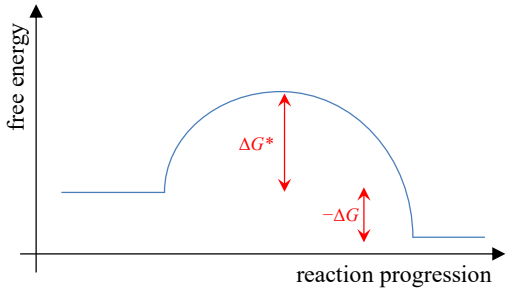
Activation Energy

Besides the free energy change of a reaction, there is also the *activation energy*.

The reaction always results in the same ΔG but the path to the final state may be associated with different barriers.

We assume there is just one barrier: After ΔG^* has been reached by a thermal fluctuation the progression is "downhill".

The backward reaction barrier is $\Delta G^* - \Delta G$!



Arrhenius Kinetics

Obviously, ΔG^* must be related to k_{on} and k_{off}, but how?

The standard model for the rate constants is Arrhenius kinetics. In its simplest form:

$$k \propto \exp\left(-\frac{\Delta G^*}{k_B T}\right)$$

A prefactor is needed that describes, for instance, the number of collisions per time and concentration if several molecules need to meet. It will also be temperature dependent!

The exponential factor is then the probability that the complex formed upon a collision actually results in the product.

In principle, Arrhenius formula applies to both k_{on} and k_{off} but the prefactor must be different for a dissociation reaction.

Eyring Equation

The Eyring equation from *transition state theory* can give rate constants more explicitly:

$$k = \frac{k_B T}{h}\exp\left(-\frac{\Delta G^*}{k_B T}\right) = \frac{k_B T}{h}\exp\left(\frac{\Delta S^*}{k_B}\right)\exp\left(-\frac{\Delta H^*}{k_B T}\right)$$

Here Planck's constant $h = 6.626\times10^{-34}$ Js comes into play since the model is actually based on quantum mechanics.

A bit of a magical model, spits out absolute numbers just from activation energy… But often a "correction" factor is used for this equation in practice!

Binding to a Surface

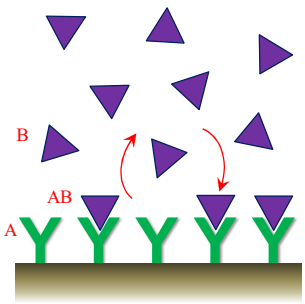
Let us say the A "molecules" are stuck to a surface. We can write $C_A + C_{AB} = C_{Atot}$ (constant), i.e. an A molecule "site" can be either free or occupied.

An equilibrium will be established where a fraction of A molecules will have B bound.

We introduce *surface coverage* Γ of the complex AB (number of molecules per area).

There will be a maximum coverage Γ_{max} corresponding to the coverage of A molecules (constant), which corresponds to C_{Atot}.

Each A molecule (or each bound B molecule) will effectively occupy an area of $1/\Gamma_{max}$.



Reaction Kinetics in Two Dimensions

Important: The A "molecules" can be any kind of binding sites on a surface. It can even be just the empty area needed to fit one B molecule. The math will be the same:

$$\frac{\partial C_{AB}}{\partial t} = k_{on}[\underbrace{C_{Atot} - C_{AB}}_{C_A}]C_B - k_{off}C_{AB}$$

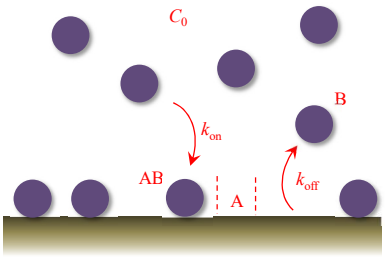
If both sides are multiplied with the thickness of the layer:

$$\frac{\partial \Gamma(t)}{\partial t} = k_{on}C_B[\Gamma_{max} - \Gamma(t)] - k_{off}\Gamma(t)$$

Assume there is a "steady supply" of B so that $C_B = C_0$ (constant):

$$\boxed{\frac{\partial \Gamma(t)}{\partial t} = k_{on}C_0[\Gamma_{max} - \Gamma(t)] - k_{off}\Gamma(t)}$$

Langmuir differential equation



$$\frac{\partial f(t)}{\partial t} = k_{on}C_0[1 - f(t)] - k_{off}f(t)$$

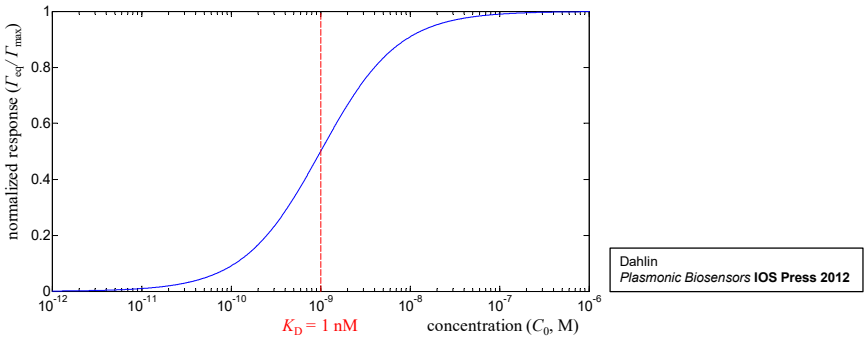
rewritten with fractional coverage $f = \Gamma/\Gamma_{max}$

Langmuir Equilibrium

As time goes we get:

$$\left\{\frac{\Gamma}{\Gamma_{\max}}\right\}_{t\to\infty} = \frac{C_0}{C_0 + K_D}$$

Hence, at equilibrium the fractional coverage f depends on C_0 and the dissociation constant K_D!



Langmuir Kinetics

Typical initial condition for *association*: $\Gamma(0) = 0$ (empty surface)

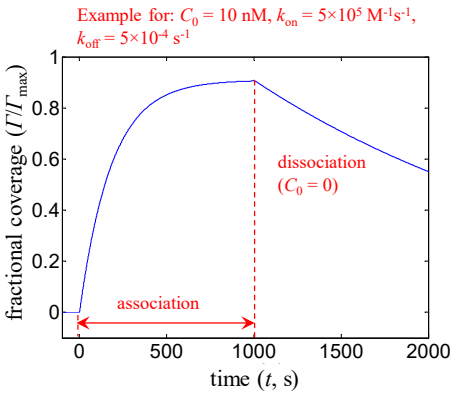
Ordinary first order differential equation, solution is:

$$\Gamma(t) = \frac{\Gamma_{\max} k_{on} C_0}{k_{on} C_0 + k_{off}} [1 - \exp(-[k_{on} C_0 + k_{off}]t)]$$

Boundary condition for *dissociation*:
$\Gamma(0) = \Gamma_0$

The solution is then, if $C_0 = 0$:

$$\Gamma(t) = \Gamma_0 \exp(-k_{off} t)$$

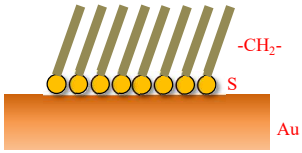


Irreversible Binding

In many cases, molecular adsorption to a surface is *irreversible* ($k_{off} = 0$). The kinetics are similar:

$$\Gamma(t) = \Gamma_{max}[1 - \exp(-k_{on}C_0 t)]$$

Here Γ will always reach Γ_{max} eventually.



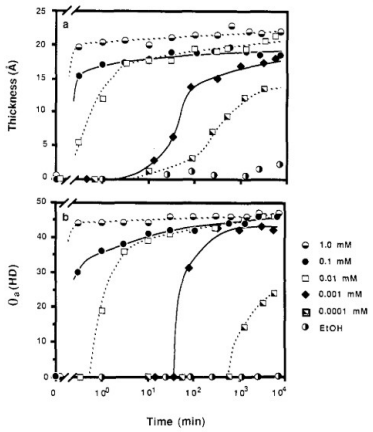


Figure 9. Kinetics of adsorption of octadecanethiol from ethanol as a function of concentration: (a) ellipsometric thickness, (b) advancing contact angle of hexadecane (HD). EtOH (●) indicates pure ethanol conaining no thiol.

Bain et al.
Journal of the American Chemical Society **1989**, 111 (1), 321-335.

Binding Kinetics Give More Information

It is possible to have the same $K_D = k_{off}/k_{on}$ but completely different rate constants!

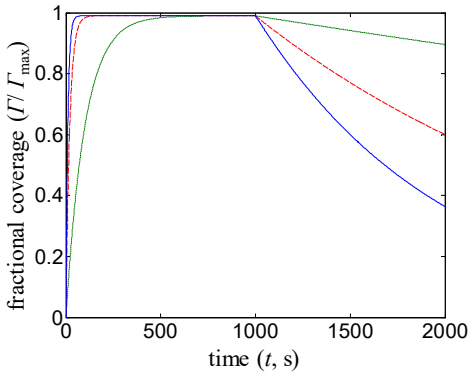
To determine k_{on} and k_{off} we need to see how Γ varies with time, not only the equilibrium value!

$k_{on} = 10^6\ s^{-1}M^{-1}$
$k_{off} = 10^{-3}\ s^{-1}$

$k_{on} = 5\times10^5\ s^{-1}M^{-1}$
$k_{off} = 5\times10^{-4}\ s^{-1}$

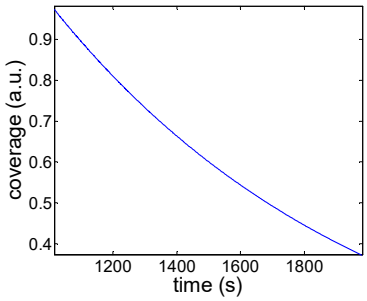
$k_{on} = 10^5\ s^{-1}M^{-1}$
$k_{off} = 10^{-4}\ s^{-1}$

fixed C_0 = 100 nM & K_D = 1 nM



Exercise 2.1

Part of an ordinary dissociation process of molecules leaving a surface is shown for an interaction with $K_D = 10^{-10}$ M. Estimate k_{on}!



Exercise 2.1

The dissociation phase is just an exponential decay which can be written:

$$\Gamma(t) = \text{constant} \times \exp(-k_{\text{off}} t)$$

We can take two values from the graph, for example:
$\Gamma_1 = 0.8$ at $t_1 = 1200$ s
$\Gamma_2 = 0.4$ at $t_2 = 1900$ s

This gives k_{off} and then k_{on} (note units):

$$\frac{\Gamma_1}{\Gamma_2} = \frac{\exp(-k_{\text{off}} t_1)}{\exp(-k_{\text{off}} t_2)} = \exp(k_{\text{off}}[t_2 - t_1])$$

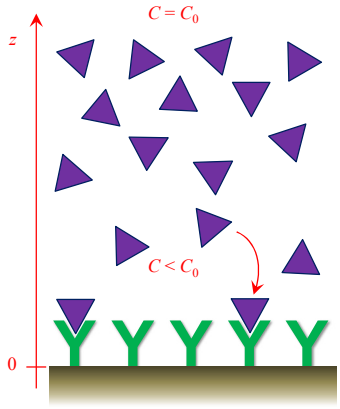
$$k_{\text{off}} = \frac{\log\left(\frac{\Gamma_1}{\Gamma_2}\right)}{[t_2 - t_1]} = \frac{\log\left(\frac{0.8}{0.4}\right)}{[1900 - 1200]} = 9.90\ldots \times 10^{-4}\text{s}^{-1}$$

$$k_{\text{on}} = \frac{k_{\text{off}}}{K_D} \approx \frac{10^{-3}\text{s}^{-1}}{10^{-10}\text{M}} = 10^{7}\text{M}^{-1}\text{s}^{-1}$$

Diffusion Controlled Binding

What if the concentration of B does not remain constant at the surface? Consider the extreme case when:

- B binds to A on the surface immediately ($k_{on} \rightarrow \infty$).
- There are infinite amounts of A ($\Gamma_{max} \rightarrow \infty$).
- The B molecules are never released ($k_{off} = 0$).



Now everything is controlled by diffusion! Fick's laws:

$$\vec{J} = -D\left[\frac{\partial C}{\partial x}\vec{x} + \frac{\partial C}{\partial y}\vec{y} + \frac{\partial C}{\partial z}\vec{z}\right]$$

$$\frac{\partial C}{\partial t} = D\left[\frac{\partial^2 C}{\partial x^2}\vec{x} + \frac{\partial^2 C}{\partial y^2}\vec{y} + \frac{\partial^2 C}{\partial z^2}\vec{z}\right]$$

J: flux in $\text{molm}^{-2}\text{s}^{-1}$ (can be mass instead of moles)
D: diffusion constant in m^2s^{-1}

One Dimensional Case

For an infinite surface in contact with an infinite solution we use Fick's second law:

$$\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial z^2}$$

Valid for:	$t > 0$ & $z > 0$
Initial condition:	$C(z, t = 0) = C_0$
Boundary condition:	$C(0, t > 0) = 0$

Scary partial differential equation! Fortunately the solution is known (homogenous Dirichlet condition in heat transport):

$$C(z,t) = \frac{C_0}{\sqrt{4\pi Dt}}\int_0^\infty \exp\left(-\frac{[z-s]^2}{4Dt}\right) - \exp\left(-\frac{[z+s]^2}{4Dt}\right) \mathrm{d}s$$

This looks complicated, but we only need the spatial derivative of *C*:

$$\frac{\partial C}{\partial z} = \frac{C_0}{\sqrt{4\pi Dt}}\int_0^\infty -\frac{[z-s]}{2Dt}\exp\left(-\frac{[z-s]^2}{4Dt}\right) + \frac{[z+s]}{2Dt}\exp\left(-\frac{[z+s]^2}{4Dt}\right) \mathrm{d}s$$

Ilkovic Equation

Further, at the surface we have $z = 0$:

$$\left\{\frac{\partial C}{\partial z}\right\}_{z=0} = \frac{C_0}{\sqrt{4\pi Dt}} \int_0^\infty \frac{s}{2Dt} \exp\left(-\frac{s^2}{4Dt}\right) + \frac{s}{2Dt} \exp\left(-\frac{s^2}{4Dt}\right) \mathrm{d}s$$

Looking closer, we see that this integral can actually be solved:

$$\left\{\frac{\partial C}{\partial z}\right\}_{z=0} = \frac{C_0}{\sqrt{4\pi Dt}} \left\{-2 \exp\left(-\frac{s^2}{4Dt}\right)\right\}_{s=0}^{s\to\infty} = \frac{C_0}{\sqrt{4\pi Dt}} [0 + 2] = \frac{C_0}{\sqrt{\pi Dt}}$$

The surface coverage is the integral in time of the incident flux J (Fick's first law):

$$\Gamma(t) = \int_0^t J(z = 0, s)\mathrm{d}s = \int_0^t D \left\{\frac{\partial C(z,s)}{\partial z}\right\}_{z=0} \mathrm{d}s = \int_0^t D \frac{C_0}{\sqrt{\pi Ds}} \mathrm{d}s = \left\{2C_0 \sqrt{\frac{Ds}{\pi}}\right\}_{s=0}^{s=t}$$

The last integral gives:

$$\Gamma(t) = 2C_0 \sqrt{\frac{Dt}{\pi}}$$

Ilkovic equation (diffusion controlled binding)

Ilkovic Kinetics

We only need the bulk concentration and the diffusion constant of the molecule to get Γ.
We can ignore the rate constants!

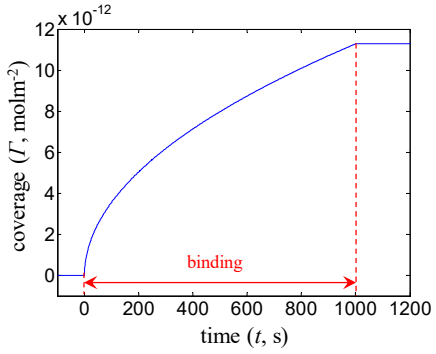
Unfortunately, the model is unrealistic:
Coverage increases indefinitely!
No dissociation!

The model can normally only describe the initial phase of a binding curve. (It was originally derived for electrochemistry.)

Extension of depletion zone is (we can kind of see how it appears in $C(z,t)$):

$$\bar{z} = \sqrt{2Dt}$$

In other words, Einstein's equation for 1D Brownian motion! (2D: 2→4, 3D: 2→6)



Example for: C_0 = 10 nM, $D = 10^{-9}$ m^{2}s^{-1}

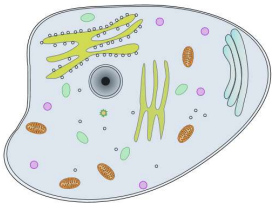
Estimating Diffusion Constants

Validity of the Ilkovic model depends on diffusion timescale, which should be slow compared to attachment rate. If it is valid we can relate C_0 and Γ, but we need to know D!

We can estimate D from Einstein-Stokes equation: $$D = \frac{k_B T}{6\pi\eta R}$$

η: dynamic viscosity (10^{-3} Pas for water)
R: radius (of the sphere)

Experimentally:
Protein D ~10^{-10} m^2s^{-1} (in pure water)
Ions D ~10^{-9} m^2s^{-1} (in pure water)
Not a huge difference!



How far does a typical molecule diffuse by random walk?
~10 µm during 1 s
~100 µm during 1 min
But diffusing 1 mm takes over 1 h…

Exercise 2.2

How long time would it take to reach a coverage of 100 ng/cm^2 on a planar surface in contact with a (very large) liquid that has a concentration of 5 fM of a 20 kDa protein with a diffusion constant of 10^{-6} cm^2/s? (Assume the protein attaches directly to the surface when reaching it.) What is the areal coverage in percent if the protein molecules are cubes with a side of 2 nm?

Use the Ilkovic equation!

Exercise 2.2

You should be able to see from the description that this is a problem where the Ilkovic equation can be used. The main challenge is to convert units! If we go for SI standard:
$C_0 = 5\times10^{-15}$ molL^{-1} = 5×10^{-12} molm^{-3}
$M = 20$ kgmol^{-1}
$D = 10^{-6}$ cm^{2}s^{-1} = 10^{-10} m^{2}s^{-1}
$\Gamma = 100$ ngcm^{-2} = 100×10^{-12} kgcm^{-2} = 100×10^{-8} kgm^{-2}

Note that the concentration must be based on kg now (multiply with M). Ilkovic gives:

$$t = \frac{\pi}{D}\left[\frac{\Gamma}{2C_0M}\right]^2 = \frac{\pi}{10^{-10}}\left[\frac{10^{-6}}{2\times5\times10^{-12}\times20}\right]^2 = 7.85\ldots\times10^{17}\text{s}$$

This is approximately 2.5×10^{10} years, more than the age of the Universe. (Comments?)

Exercise 2.2

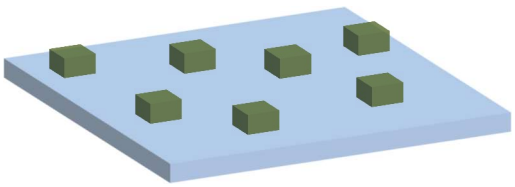
To get the coverage, take for instance the number of molecules on 1 m^2:

100 ngcm^{-2} = 10^{-3} gm^{-2}
10^{-3} g / 20000 gmol^{-1} × N_A mol^{-1} = 3×10^{16} molecules

The area that a molecule occupies is $[2\times10^{-9}]^2$ m^2.

The area of that many cubic molecules is $3\times10^{16}\times[2\times10^{-9}]^2 = 0.12$ m^2

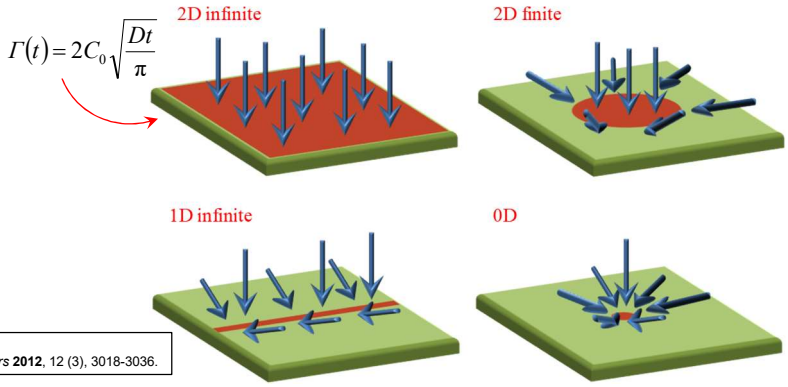
The coverage is thus 12%.



Influence From Geometry

The infinite planar surface (Ilkovic) scenario represents the case of diffusive transport which gives the lowest surface coverage after a certain time.

If the surface can "suck in" molecules from more directions the flux is enhanced!



Dahlin
Sensors **2012**, 12 (3), 3018-3036.

Disappearance of Depletion Zone

For a sufficiently small spot, the depletion becomes insignificant because new molecules can diffuse in so efficiently.

Solving the equivalent of Ilkovic in spherical coordinates gives (no derivation):

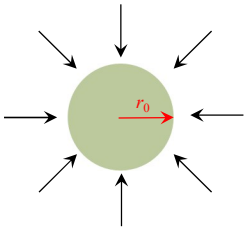
$$J(r = r_0) = C_0 D\left[\frac{1}{r_0} + \frac{1}{\sqrt{\pi D t}}\right]$$

By comparing the radius of the spherical surface with the characteristic diffusion distance it can be seen that the $1/r_0$ term will typically dominate already after very short time. Thus:

$$\Gamma \approx \frac{C_0 D t}{r_0}$$

Linear with t!

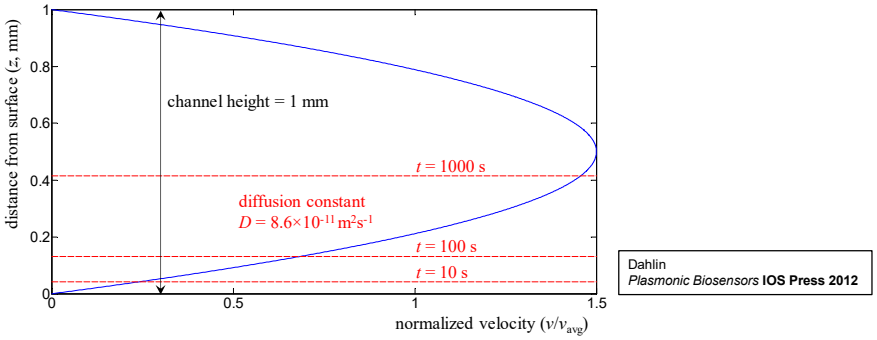
Important for electrochemistry with microelectrodes (constant current predicted).



Flow

Concentration gradients can be eliminated by *convection* in the liquid. It is generally not hard to ”access” the depletion zone and “deliver” molecules efficiently. One can often reach Langmuir behavior by continuous liquid flow!

Note that the molecules in solution never “sense” the surface until they adsorb. Their movement is controlled only by diffusion and convection.

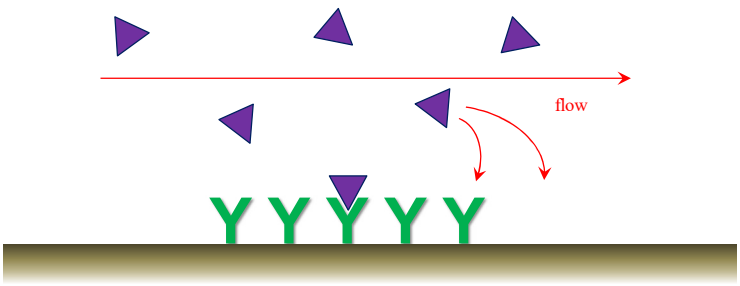


Capture Efficiency

For diffusion limited binding in combination with flow (relatively uncommon) the binding rate increases with volumetric flow rate Q:

$$\frac{\partial \Gamma}{\partial t} \propto Q^{1/3} \qquad \text{(for high } Q\text{)}$$

However, the *capture efficiency* goes down because at high Q each molecule (in solution) spends a very short time near the receptors (on the active region of the surface).



Combining Reaction, Convection and Diffusion

In many cases, all effects must be taken into account, i.e. reaction, diffusion and convection. This requires numerical methods!

Some dimensionless numbers are used to characterize which effect dominates. The *Peclet number* is the ratio between diffusive time and convective time:

$$\mathrm{Pe} = \frac{\frac{x^2}{D}}{\frac{x}{v}} = \frac{vx}{D}$$

Here v is the liquid flow velocity and x is the "characteristic distance" of interest, such as the size of a binding spot.

The *Damköhler number* is the ratio between reactive flux and diffusive flux:

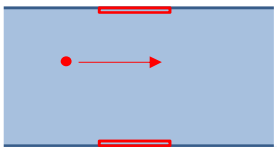
$$\mathrm{Da} = \frac{k_{\mathrm{on}}\Gamma_{\mathrm{max}}C_0}{D \times \frac{C_0}{z}} = \frac{k_{\mathrm{on}}\Gamma_{\mathrm{max}}z}{D}$$

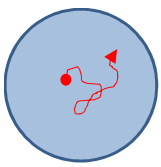
Here z is the characteristic depletion zone thickness (which depends on Pe).

Exercise 2.3

A 100 nm virus flows in a 100 µm diameter tube with Q = 5 µL/min (water at room temperature). A region of 10 µm length in the channel with very sticky walls appears. Is the virus likely to attach to the wall or flow past this region?

Use the equation for Brownian motion!





Exercise 2.3

This is essentially a Peclet number analysis. We need the average flow velocity v_{avg} from $Q = Av_{avg}$ where A is the cross-section area of the tube.
$Q = 5\times10^{-9}/60$ m^{3}s^{-1}
$A = \pi[50\times10^{-6}]^2$ m^2

$$v_{\text{avg}} = \frac{5 \times 10^{-9}/60}{\pi[50 \times 10^{-6}]^2} \approx 0.01 \text{ m/s}$$

So it takes on the order of 10×10^{-6} / 0.01 = 10^{-3} s to flow past the sticky region. How long does the virus diffuse radially during this time? First get D from Einstein-Stokes:

$$D = \frac{k_B T}{6\pi\eta R} = \frac{1.38 \times 10^{-2} \times 300}{6\pi \times 10^{-3} \times 50 \times 10^{-9}} \text{ m}^2\text{s}^{-1}$$

For water at 300 K, $\eta = 10^{-3}$ Pas. The expected diffusion length in 2D is $[4Dt]^{1/2}$. We get $D = 4.4\times10^{-12}$ m^{2}s^{-1} and a radial diffusion distance of 1.3×10^{-7} m during 1 ms.

Since the virus diffuses less than 1 µm during the time it flows by it will most likely not bind because the channel is much wider than this. (We have Pe >>1.)

Patterning

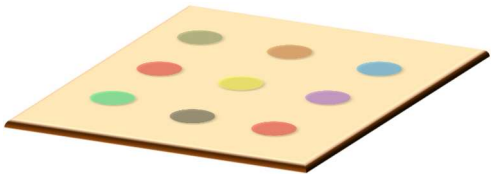
How can we put different molecules on different places on the surface? Why should we?

• Investigate how something in solution to stick to the surface when it is modified in different ways, several measurements at once.

• Reduce active area in an experiment.

• Enhance diffusive flux.

• See how cells attach and grow on patterns.



Microdispensing

Most straightforward patterning is to dispense small droplets (like a printer).

- Droplets dry in seconds unless humidity is controlled.
- Excess molecules need to be washed away.
- Contact angle will be very important for spot size.

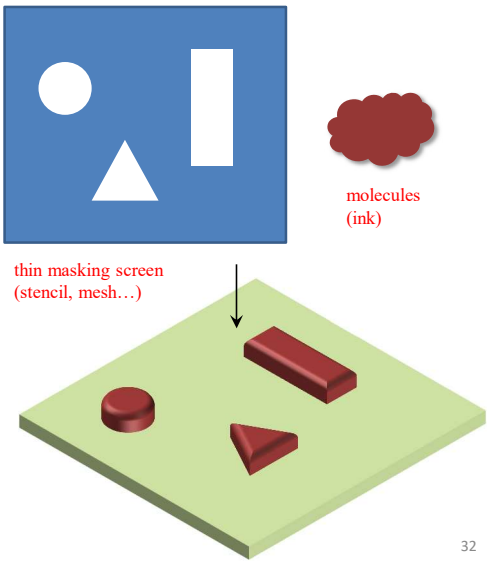
Microdrop Technologies
http://www.microdrop.de

$20\ \text{pL} = 20 \times 10^{-15}\ \text{m}^3 = 2 \times 10 \times 10 \times 10\ \mu\text{m}^3$

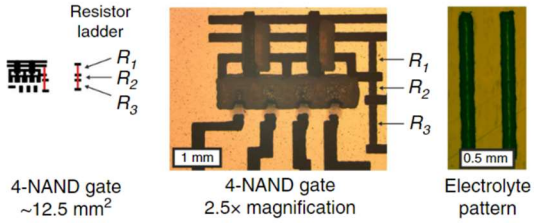
Screen Printing

Very simple and efficient (parallel).

Resolution is not great.



New design and high-quality screen printing tools



Andersson-Ersman et al.
Nature Communications **2019**, 10 (1), 5053.

Material-Specific Modifications

If we have a surface with a pattern of different materials, we can also make molecules bind in the same pattern!

Even if some molecules stick to the wrong surface, they are probably not covalently bound and can be removed by washing with solvents or detergents.

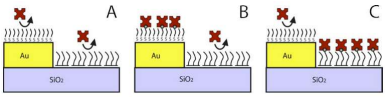


FIG. 1. Schematic description of the surface modification. (A) Gold was coated using thiol-modified PEG carrying a terminal hydroxyl group. Silicon dioxide was coated with PLL-*g*-PEG, a copolymer adsorbing electrostatically through its polylysine backbone, thus exposing its PEG chains toward the suspension. Both surfaces are shown to be inert to streptavidin and serum finding. When using the biotinylated form of either of the PEG coatings, streptavidin could be selectively bound to either gold (B) or SiO_2 (C).

Marie et al.
Biointerphases **2006**, 2 (1), 49-55.

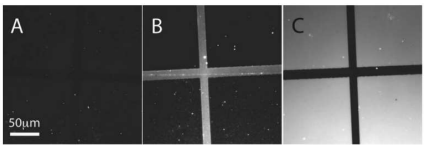


FIG. 2. Fluorescence micrographs (filters chosen for Cy3 emission) of 13 μm wide lines of gold on a SiO_2 substrate. The images were recorded after the addition of streptavidin labeled with Cy3. Gold and SiO_2 were coated, respectively, with (A) thiol-PEG and PLL-*g*-PEG, (B) thiol-PEG/PEGbiotin and PLL-*g*-PEG, and (C) thiol-PEG and PLL-*g*-PEG/PEGbiotin. All images have identical contrast and brightness settings; the scale shown in (A) is the same for (B) and (C). The bright spots in the micrographs are attributed to surface defects.

Electrochemical Patterning

An electrochemical potential can control bond formation to metals.

Pattern individual electrodes even at nanoscale separation.

So far used only for thiol desorption from gold: <50 nm gaps

$$Au\text{-}S\text{-}R + H^+ + e^- \rightarrow Au + HS\text{-}R$$

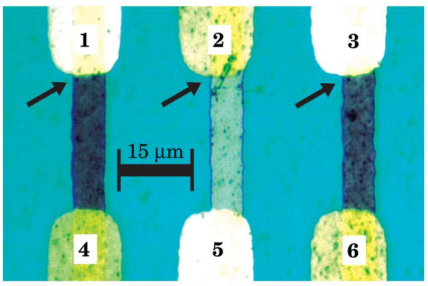
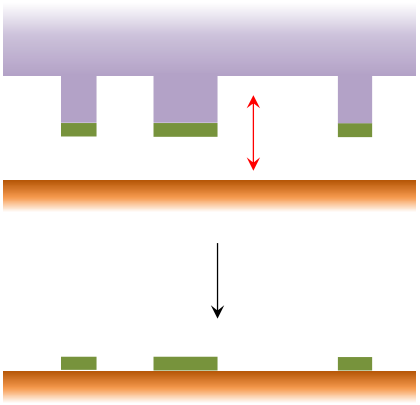


Figure 2. Optical image of the selectively coated electrode array after the detection procedure. The sub-50-nm gaps separating opposing electrodes occur at the upper junctions between the wide and narrow metal strips and are indicated by the arrows. The three narrow metal strips in the center of the picture are hence part of electrodes 4, 5, and 6. Electrodes labeled 2, 4, and 6 were coated with oligonucleotide **X** using the selective desorption technique described in the text and subsequently colored using the anti-biotin antibody detection scheme. The color contrast between the electrodes (electrodes 2, 4, and 6 are significantly darker than electrodes 1, 3, and 5) shows that a very high degree of selective coating has been achieved across the nanometer-sized gaps. Note that the narrow central stripes are initially darker than the wide features owing to the metal layer being thinner there.

Tencer, Berini
Langmuir **2008**, 24 (21), 12097-12101.

Contact Printing

Stamp transfers molecules to surface.



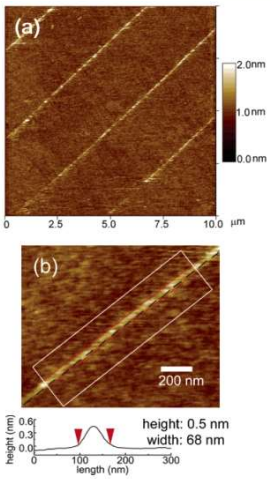


Figure 4. AFM images of printed titin multimer protein lines on silicon surface (a) at large scale and (b) at high-resolution with average cross section below.

Li et al.
Langmuir **2003**, 19 (6), 1963-1965.

Atomic Force Microscopy Writing

Nanoscale pen and ink!

Limitations for type of molecule and "ink" solution…

Can also "shave".

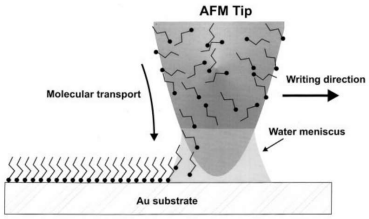
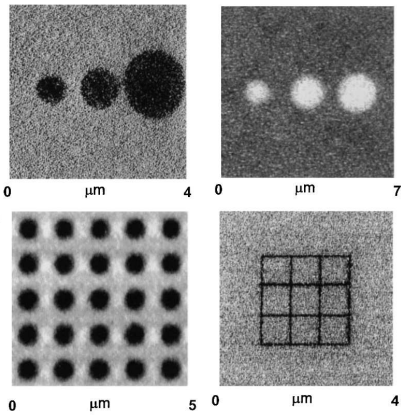


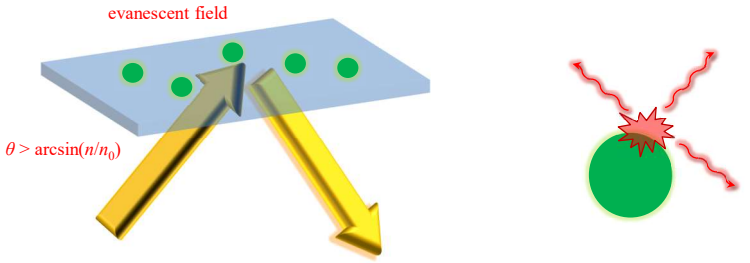
Fig. 1. Schematic representation of DPN. A water meniscus forms between the AFM tip coated with ODT and the Au substrate. The size of the meniscus, which is controlled by relative humidity, affects the ODT transport rate, the effective tip-substrate contact area, and DPN resolution.

Piner et al.
Science **1999**, 283 (5402), 661-663.



Verification of Patterns

Molecules are normally hard to see. Patterns with resolution down to ~1 µm can be imaged by fluorescence if there is a *label* on the bound molecules.



Reducing the excitation and collection volume is key to detect single molecules. This can be done by *total internal reflection* illumination on transparent materials. Signal comes only from molecules ~100 nm or closer to the surface.

Confocal may also be an option but it is more intended for 3D imaging and operates by scanning.

Checklist 2

- Reversible and irreversible binding
- Langmuir model and equilibrium
- Ilkovic model and diffusion
- Influence from geometry of "binding spot"
- Influence from convection (flow)
- How to make patterns on the microscale
- How to make patterns on the nanoscale
- How to verify pattern formation

Exercise 2.4

A surface with receptors becomes covered with targets according to the Langmuir equation with $k_{on} = 10^5$ $M^{-1}s^{-1}$ and $k_{off} = 10^{-4}$ s^{-1}. There is one molecule per cubic micrometer in solution. What is the time required to reach 50% coverage?

→

101 min

Exercise 2.4

A microelectrode is used to detect neurotransmitters in the brain by electrochemical reactions. Assume the electrode is spherical with radius 10 μm and that the molecules react immediately when the reach the surface. Show that the approximation $\Gamma = C_0 Dt/r_0$ holds well already after a few seconds of measuring. (Set $D \approx 10^{-10}$ m^2/s.) What will the measured current (vs time) look like?

→

It can be calculated that $1/r_0$ is twice as high as $[\pi Dt]^{-1/2}$ after ~1 s, so the time dependent term can be removed from the solution to the PDE. The current will be constant.