Principles of Electronic Nanobiosensors

Unit 4: Selectivity

Bonus Lecture 4.4: Noise in Transducers

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Outline

- Introduction: Noise as a selectivity problem
- Types and physics of noise sources:
  - Thermal or white noise
  - Absorption-desorption
  - 1/f or pink noise
- Beating the noise limit and improving SNR
  - Resampling
  - Lock-in
- Conclusion

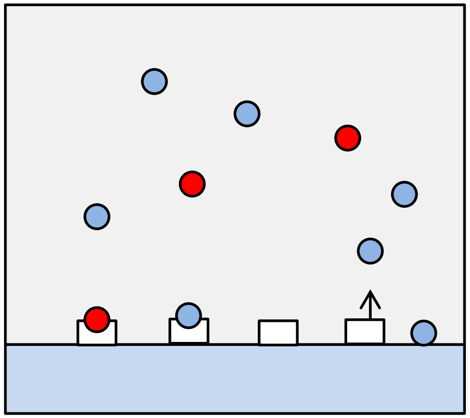
Selectivity issue due to biomolecules

Competitive binding at steady state

$$N\left(t \to \infty\right) = N_T + N_T^{'} + N_{Geom}$$

$$= \frac{k_T N_0 \rho_T}{k_T \rho_T + 1} + \frac{k_T^{'} N_0 \rho_T^{'}}{k_T^{'} \rho_T^{'} + 1} + \frac{k_p N_p \rho_p}{k_p \rho_p + 1}.$$

$$D\nabla^2 \rho = 0$$



$$\alpha = \frac{N_T}{N_T + N_T^{'} + N_{Geom}}.$$

$$\boxed{\beta = \frac{N_T^{'} + N_{Geom}}{N_T + N_T^{'} + N_{Geom}}.}$$

$$\begin{pmatrix} \alpha+\beta \\ \beta \\ \beta \\ \alpha+\beta \end{pmatrix} = \begin{bmatrix} \alpha & \beta & \beta & \beta \\ \beta & \alpha & \beta & \beta \\ \beta & \beta & \alpha & \beta \\ \beta & \beta & \beta & \alpha \end{bmatrix} \begin{pmatrix} 1 \\ 0 \\ 0 \\ 1 \end{pmatrix}$$

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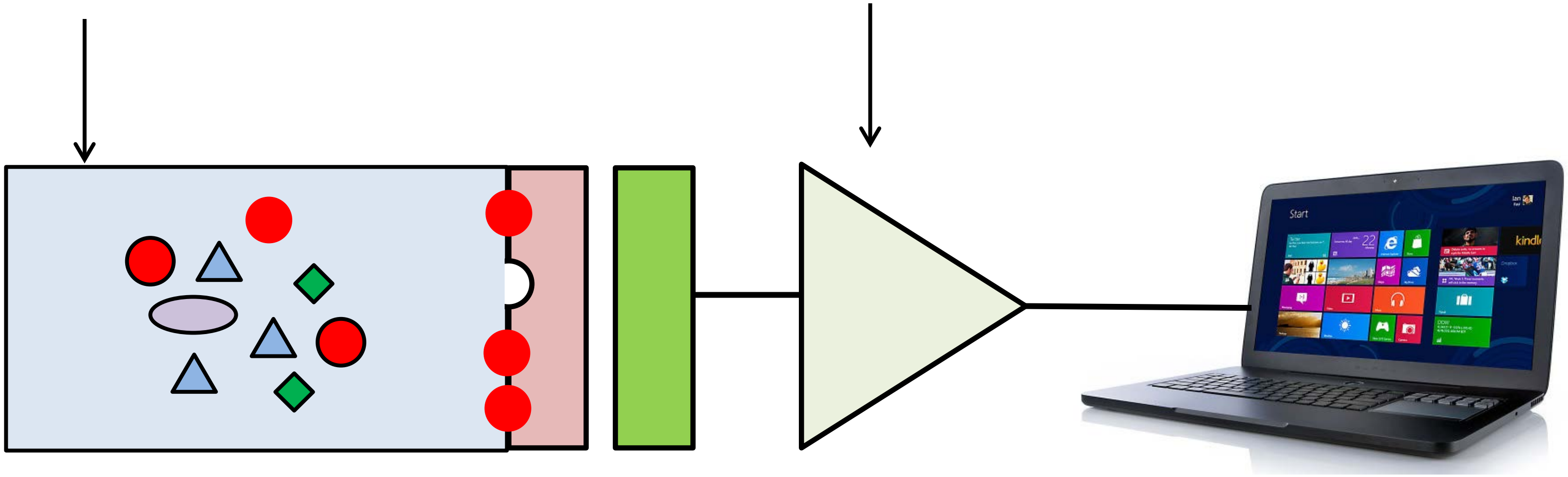
Noise is also a Selectivity Problem



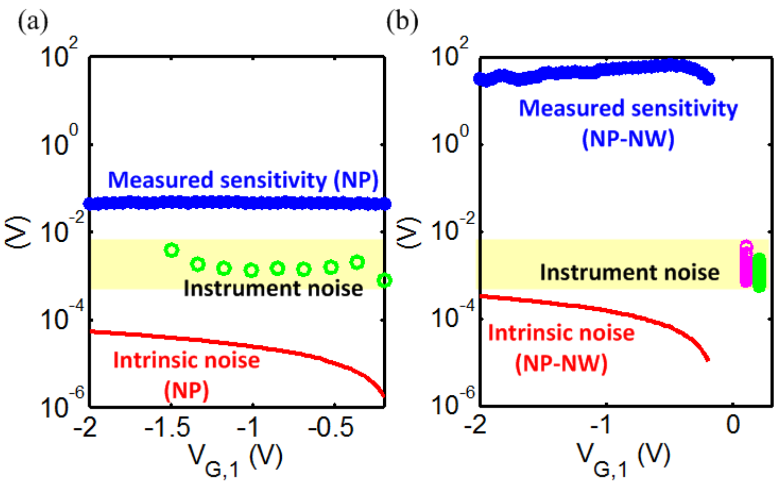
Environment Noise

Transducer Noise

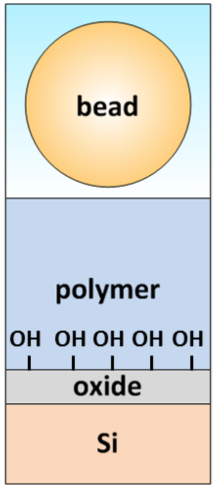
Analyte	Receptor	Transducer	Output analyzer
DNA	Antibodies	Electrical	
Protein	DNA	Optical	
Glucose	SAMs	Mechanical	

Noise in various lectures

Double-gated pH sensor



Genome sequencer



$$\delta V_G = \sqrt{\frac{q^2 k_B T N_t \lambda}{W L C_{eff}^2}\left[1+\left(\alpha \mu_{eff} C_{eff}\frac{I_{DS}}{g_m}\right)\right]\log\left(\frac{f_2}{f_1}\right)}$$

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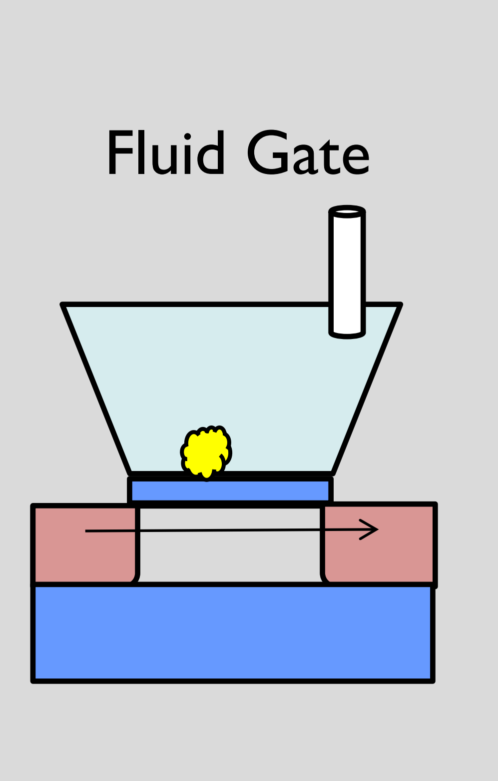
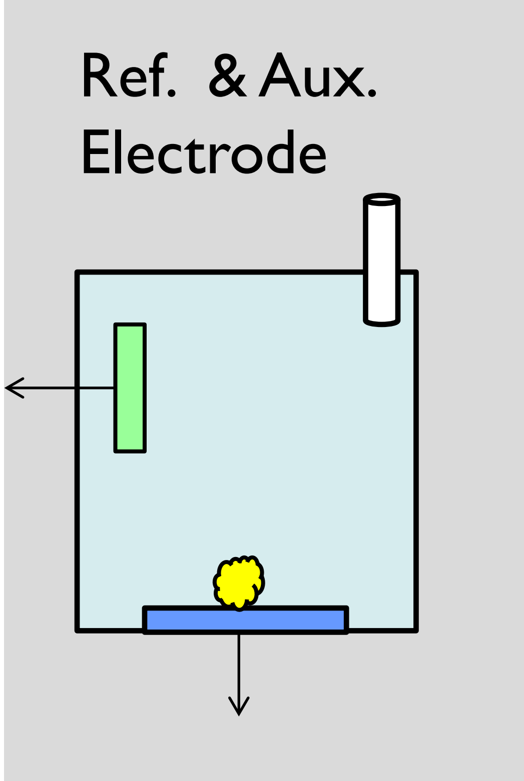
Recall: Three types of sensors

Potentiometric



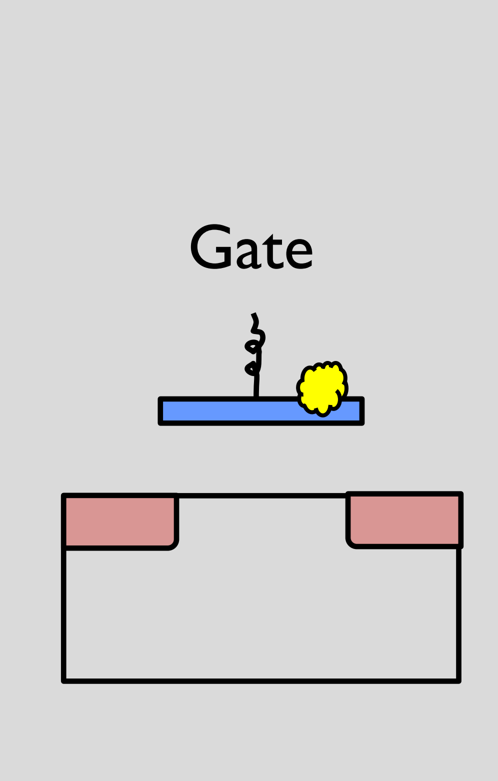
Charge to current

Amperometric



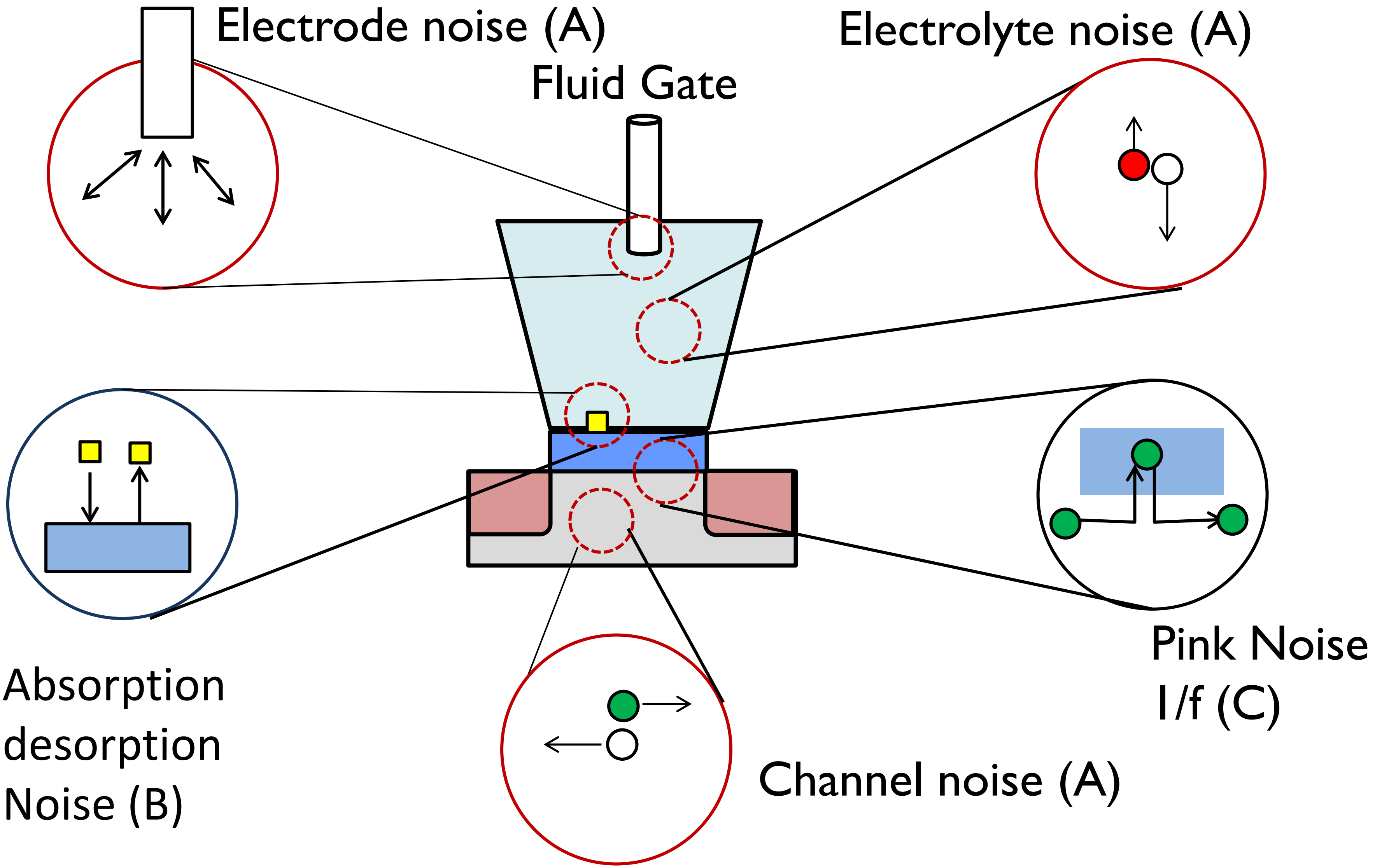
Chemical to current

Mechanical



Mass to frequency

Noise in Potentiometric Sensors



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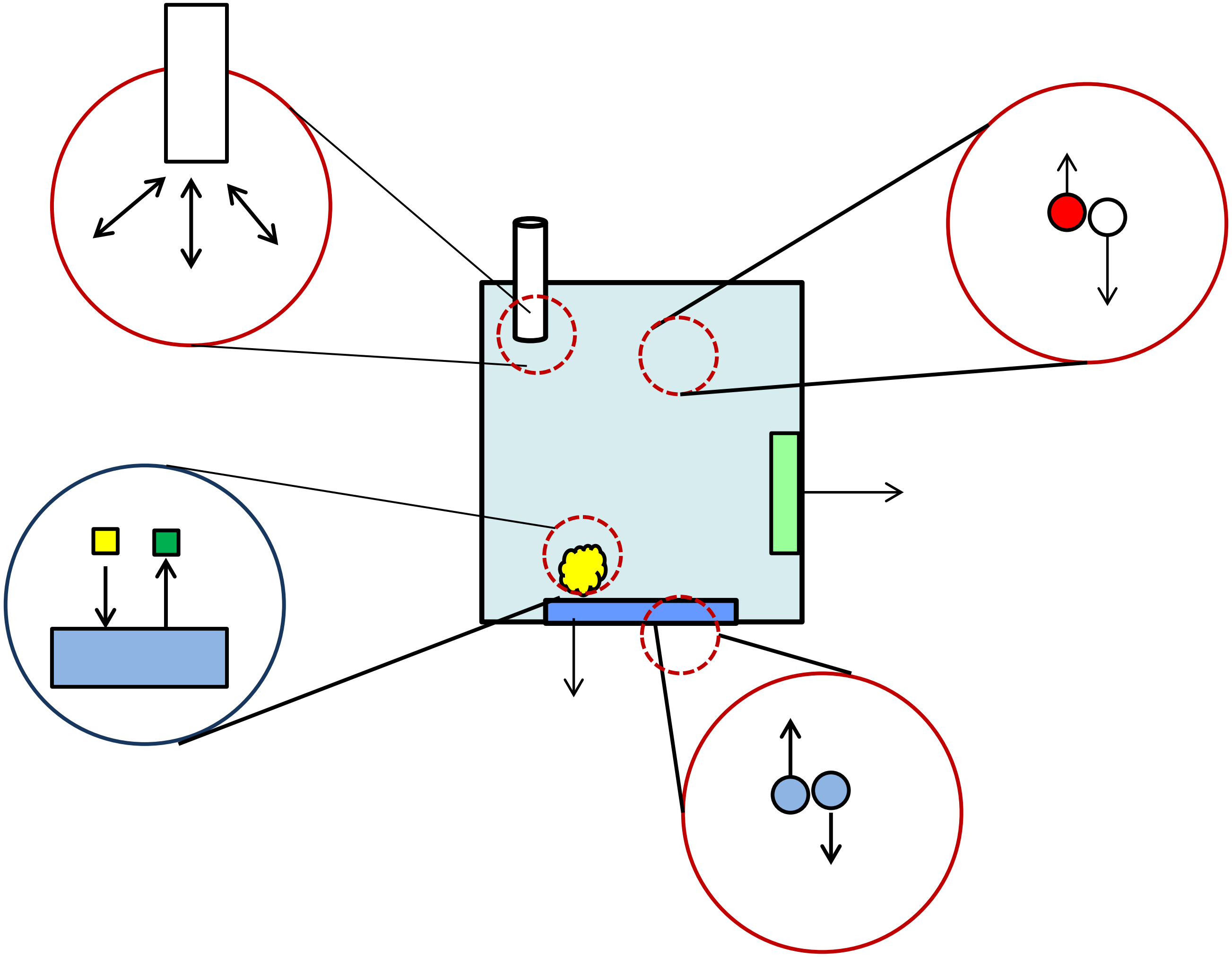
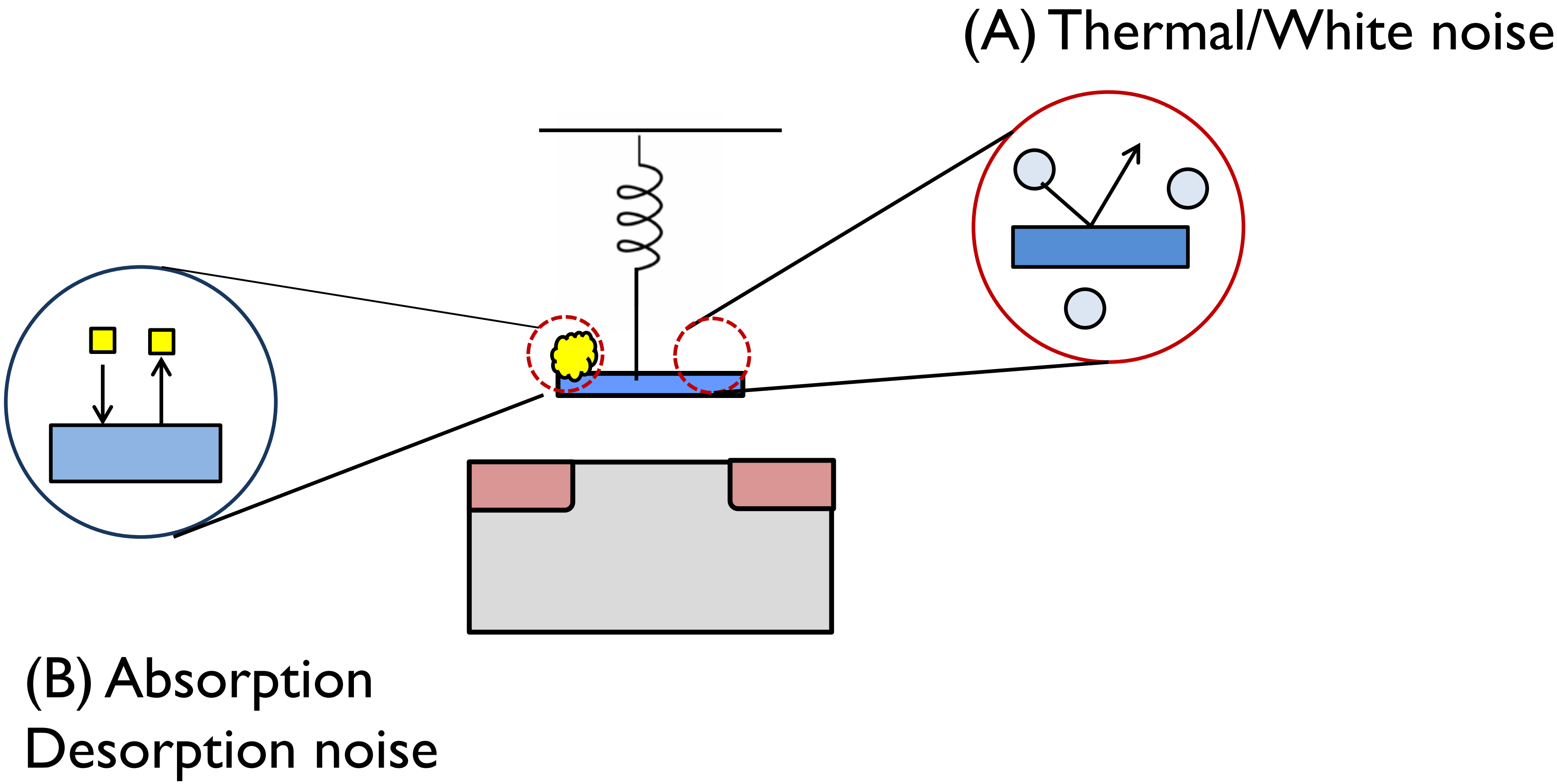
Noise in Amperometric Sensor



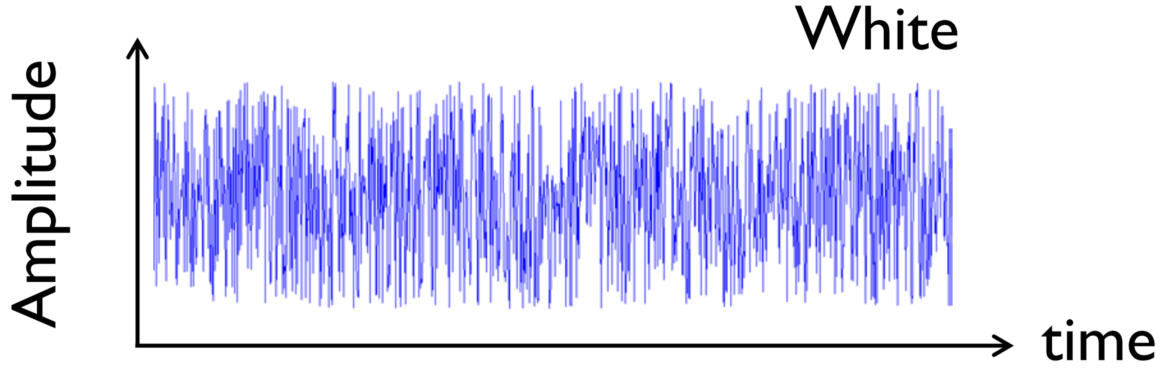
Noise in Cantilever Sensors

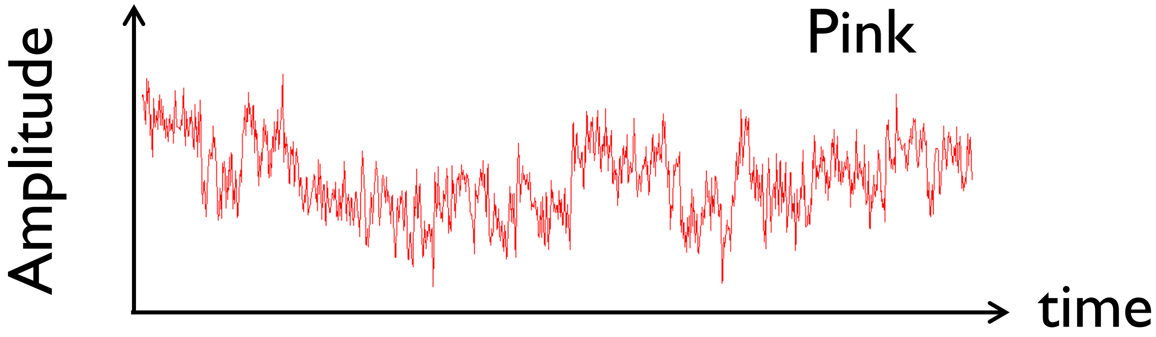


(A) Thermal/White noise

(B) Absorption
Desorption noise

White noise and Pink Noise





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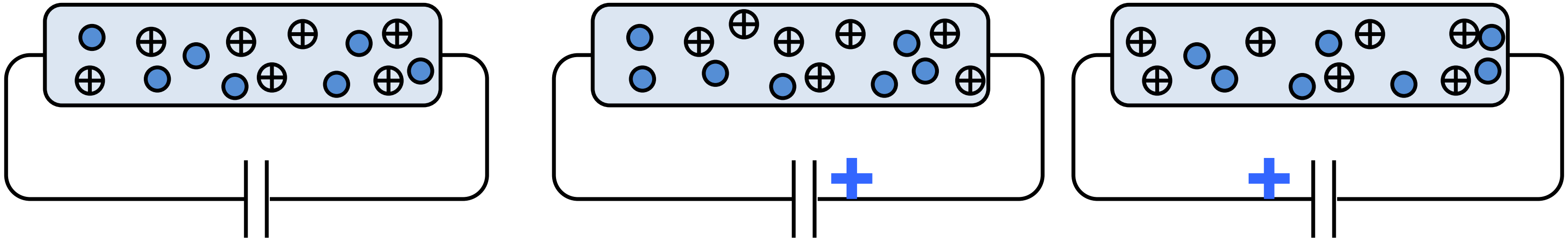
Thermal (White) Noise in a Resistor



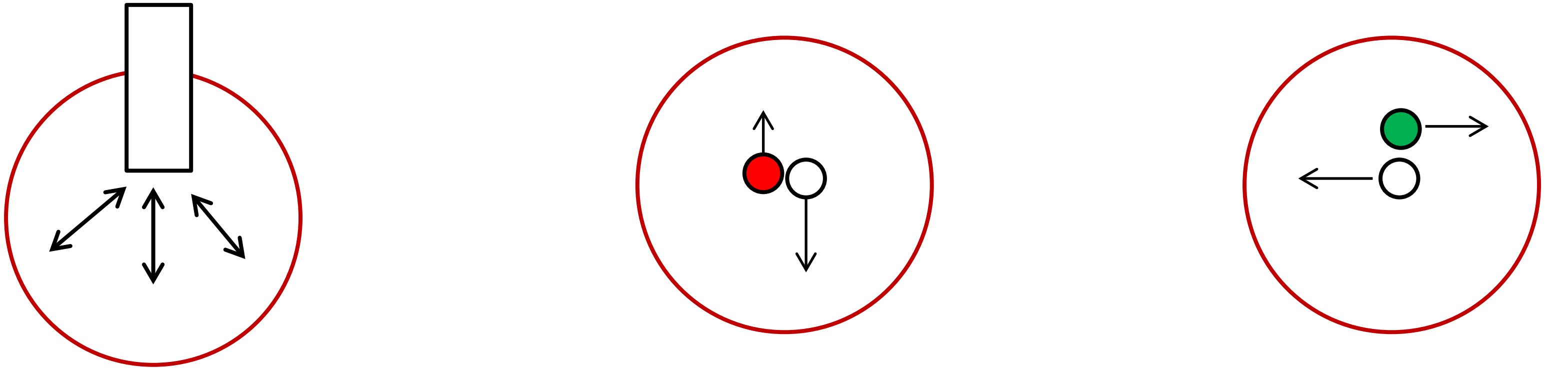
$$\frac{1}{2}CV_n^2 = \frac{k_BT}{2} \qquad V_n^2 = \frac{k_BT}{C} \qquad B \equiv f_c = \frac{1}{2\pi RC}$$

$$V_n^2 = 2\pi k_BT\,R\,B \text{ (approx!)}$$

$$= 4k_BT\,R\,B \text{ (correct)}$$

$$\Rightarrow \upsilon_n^2(f) \equiv 4k_BTR$$

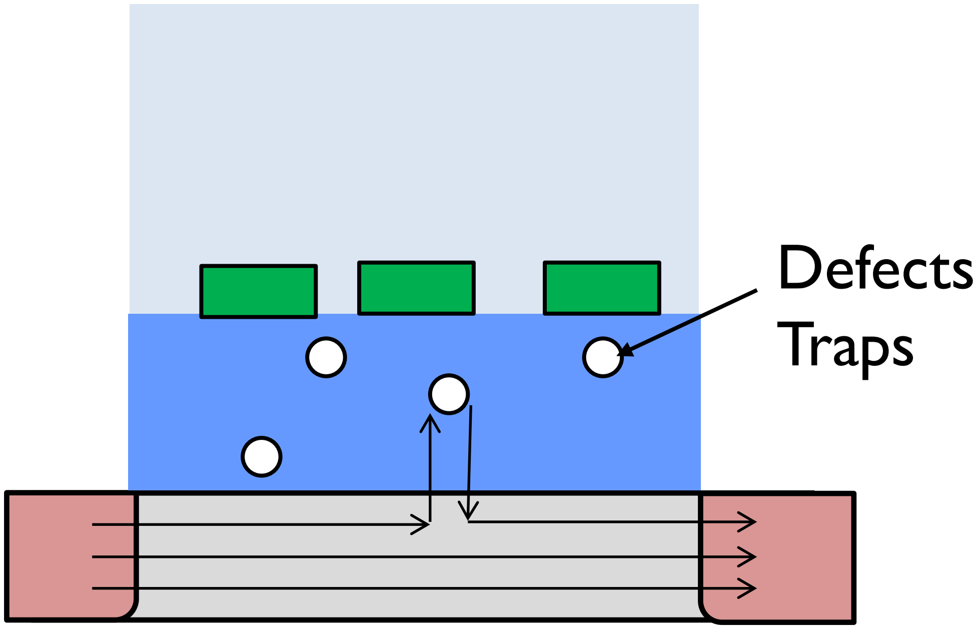
White noise from various sources

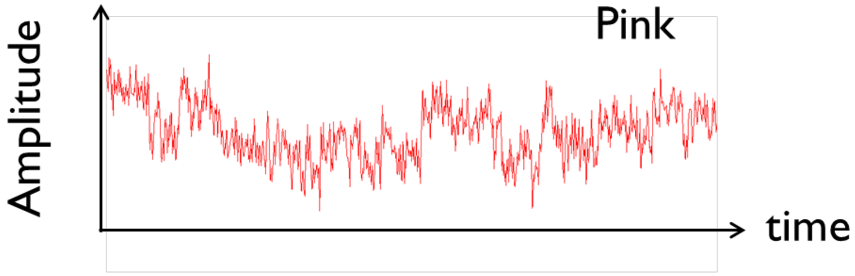


$$\upsilon_n^2(f) \equiv 4k_B T R_c \qquad \upsilon_n^2 = 4k_B T R_{sol} \qquad \upsilon_n^2 = 4k_B T R_{ch}$$

$$R_{sol} = \left(2zn_i I_0 q\mu\right)^{-1} \qquad R_{ch} = \partial I_D / \partial V_D$$

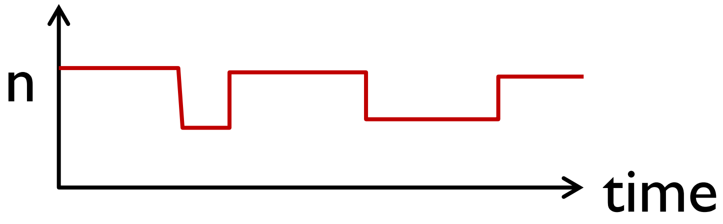
Origin of Pink Noise: Trapping/Detrapping

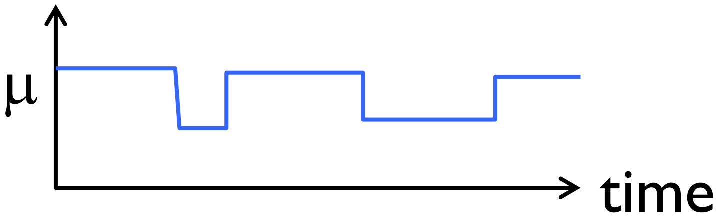




$$I_D = qn\mu E$$

$$\frac{\Delta I_D}{I_{D,0}} = \frac{\Delta n}{n_0} + \frac{\Delta \mu}{\mu_0}$$





$$\frac{\Delta I_D}{I_{D,0}} = \frac{\Delta n}{n_0} + \frac{\Delta \mu}{\mu_0}$$

1/f noise

Number fluctuation

mobility fluctuation

$$\upsilon_G^2(f) = \frac{q^2 k_B T N_T \lambda}{WL \times C_0^2}\left[1 + \alpha \mu C_0 \frac{I_D}{\partial I_D / \partial V_G}\right] \times \frac{1}{f} \equiv \frac{A^2}{f}$$

=1

$$V_{G,n}^2 = \int_{f}^{f_2} \upsilon_G^2(f) df = A^2 \ln(f_2 / f_1)$$

$$Q_n = C_0 V_{G,n}$$

$$\mathrm{SNR} = \frac{I_D}{I_n(f_1, f_2)}$$

Example of 1/f noise

W=100 nm, L=5 um, C_0=4.3 x10^{-7} F/cm^2
N_T=2.3x10^{18} eV^{-1}cm^{-3}, λ=.14 nm, a=1 (linear regime)

Number of traps

Tunneling distance

$$\upsilon_G^2(f) = \frac{q^2 k_B T N_T \lambda}{WL \times C_0^2} = 1.3\times 10^{-4}\,\frac{\mathrm{V}^2}{Hz}$$

Smaller transistors/sensors have larger noise !

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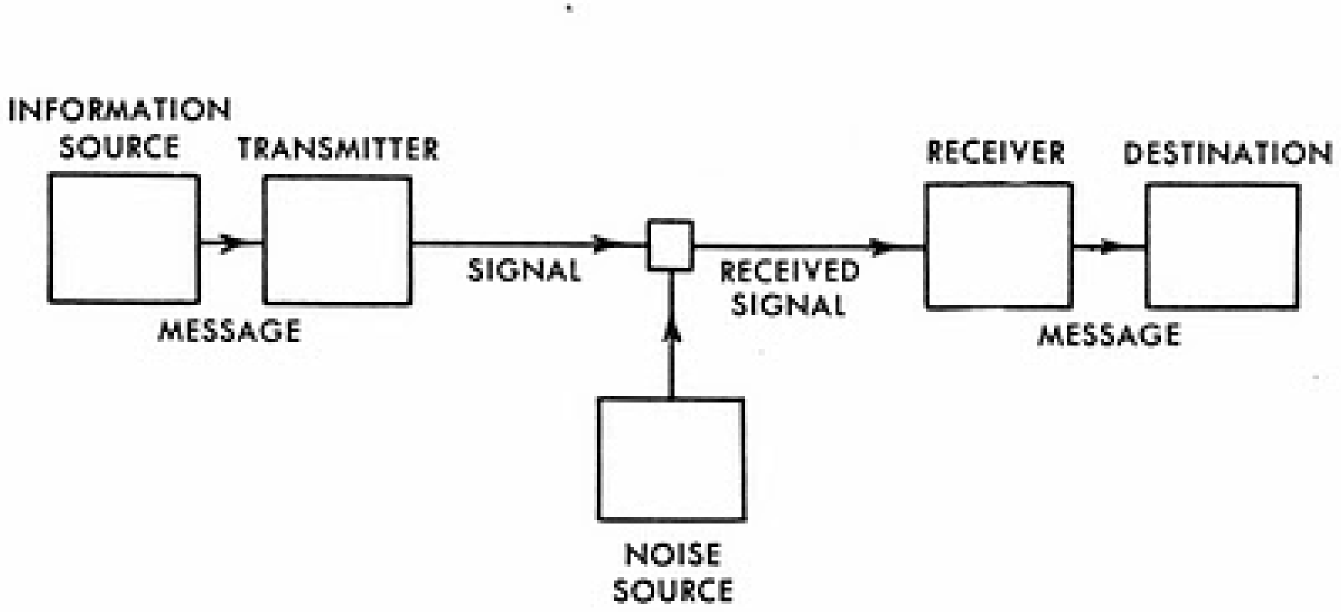
Selectivity: A problem of Information theory?

DNA sequence [1001]

Parasitic molecules
Homopolymers
Sensor noise

Sensor output

$\alpha + \beta, \beta, \beta, \alpha + \beta$



Better S/N ratio by increasing signal strength (PCR), resampling, or by suppressing the noise by tagging

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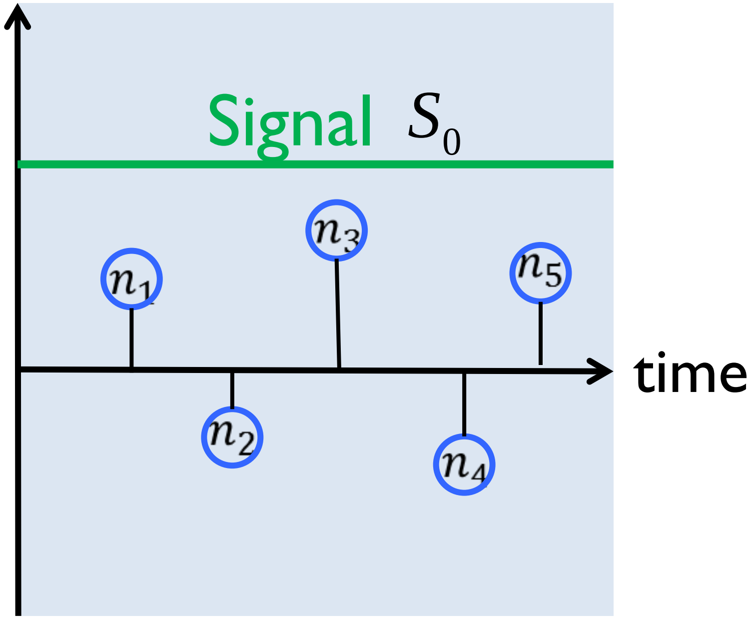
Resampling for improved SNR



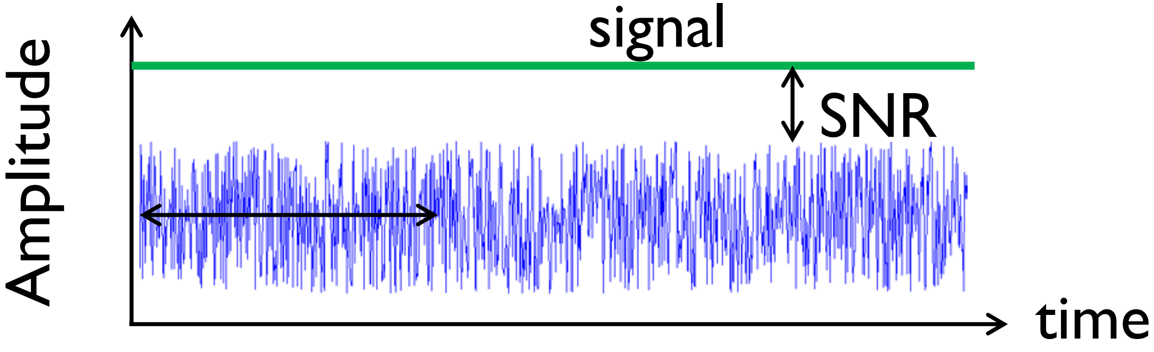
$$\frac{S_0}{n_3} < \frac{5S_0}{\sum_{i=1}^{5} n_i}$$

Trade-off Speed for accuracy

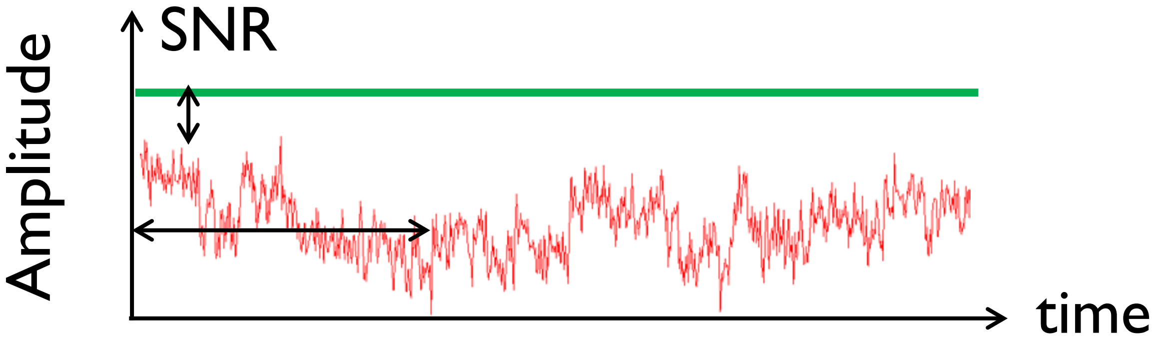
$$SNR = \frac{N \times S_0}{\sigma(N)} = \frac{N \times S_0}{\sigma_0 \sqrt{N}} = \sqrt{N}\left(\frac{S_0}{\sigma_0}\right)$$

White noise and Pink Noise

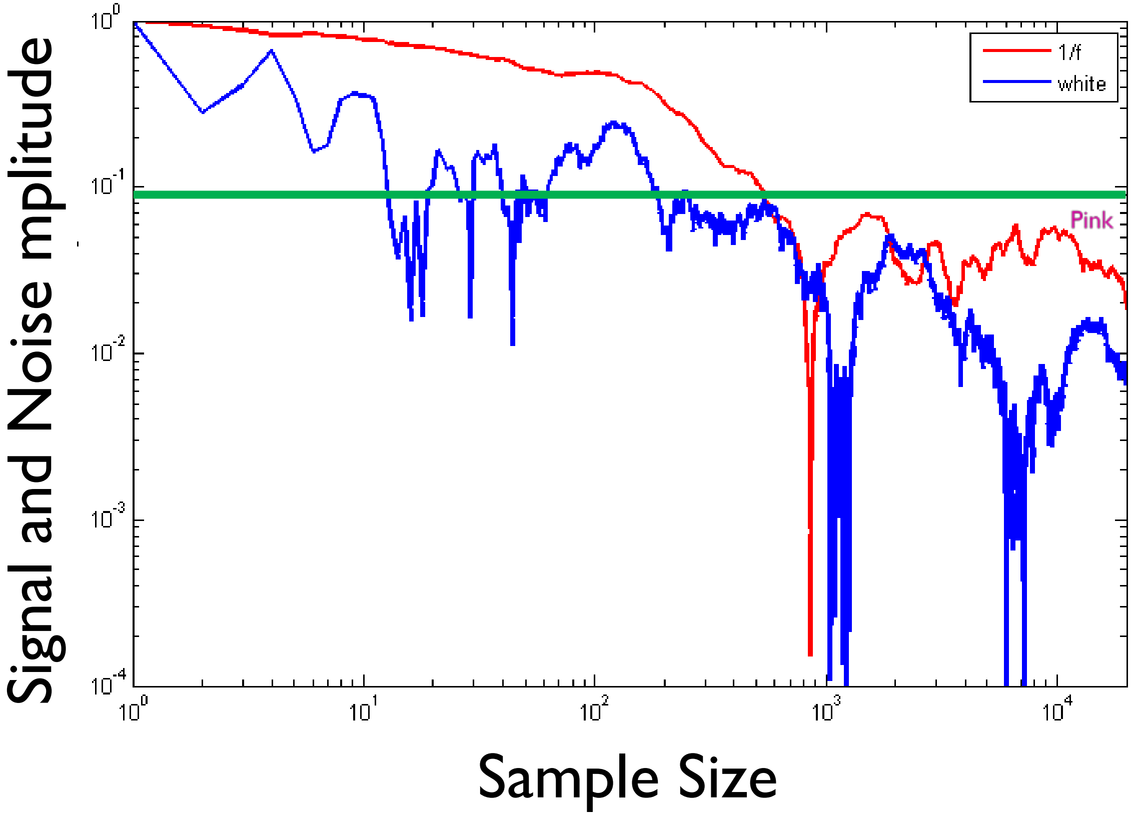
White

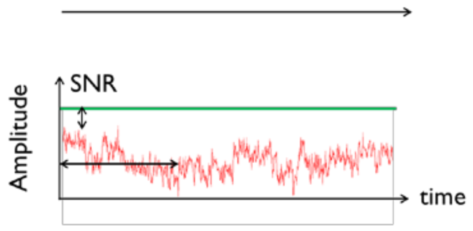


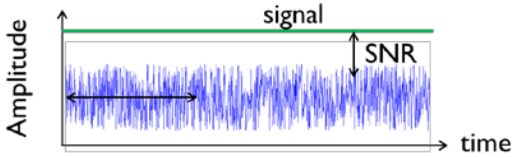
Pink



Signal averaging improves SNR dramatically







Few hundred samples are good enough

Conclusions

- We have discussed two classes of selectivity issues related to biomolecules and transducers
- Of all the noise sources in a potentiometric sensor, 1/f noise is dominant. Thermal noise play an important role in cantilever sensing.
- Analyte concentration changes slowly compared to the ability to sample the signal. This offers an opportunity to detect signal even below the instantaneous noise level.
- Careful consideration of noise is key to a robust biosensor platform.