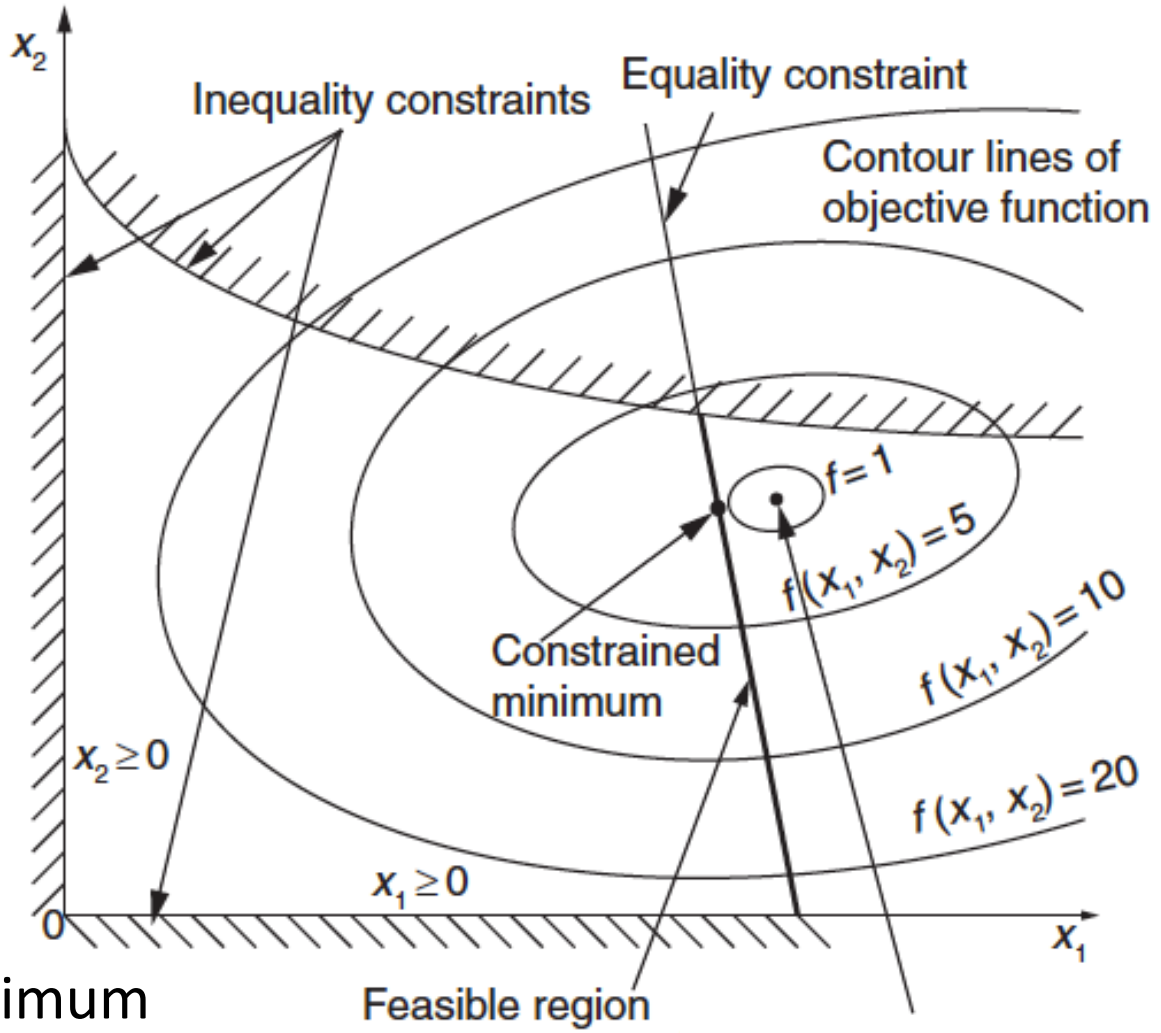
Q1: Linear least squares regression works best when the following assumptions are valid:

(pick the incorrect one)

A. The values of the independent variable x are known exactly. In other words, the error in x is much less compared to the variability in the dependent variable y.
B. The scatter of the y points about the function curve follows a Gaussian distribution.
C. The standard deviation that characterizes the variation in y is the same for all x values. In other words, the data are homoscedastic.
D. All y points are independent and are randomly distributed about the curve.
E. All of the regression parameters are positive in sign.

Q2:



A. Unconstrained minimum
B. Constrained maximum
C. Bullseye
D. Inflection point

What is the region in there?

Q3: A **multimodal function**…

A. depends on more than one variable.

B. has multiple extrema.

C. has outputs in the complex number plane.

D. is a multivalued function.

E. has a family of solutions.

Q4: Find the line with the error:

```
function newtons1Doptimization(func, x0, tolx)
% Newton's method is used to minimize an objective function of a single
% variable

% Input variables
% func : first and second derivative of nonlinear function
% x0 : initial guessed value
% tolx : tolerance in estimating the minimum
% Other variables
maxloops = 20;    A
[df, ddf] = feval(func,x0);  B
fprintf(' i x(i) f''(x(i)) f''''(x(i)) \n'); %\n is carriage return
% Minimization scheme
for i = 1:maxloops
    x1 = x0 - df/ddf;  C
    [df, ddf] = feval(func,x0);  D
    fprintf('%2d %7.6f %7.6f %7.6f \n',i,x1,df,ddf);
    if (abs(x1 - x0) <= tolx)  E
        Break
    end
    x0 = x1;
end
```

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In situ Microrheological Determination of Neutrophil Stiffening Following Adhesion in a Model Capillary

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Abstract—There has been considerable debate on the relative importance of biochemical stimuli and mechanical deformation in neutrophil adhesion in lung capillaries, a process observed following bacterial infection in the body. In contrast to venules, where the vessel diameter is larger than the leukocyte diameter (6–9 μm) and the adhesion process is better understood, in lung capillaries the vessel diameter (2–8 μm) is smaller than the leukocyte diameter. In this study, a micropipette was used as a model for the alveolar capillary microcirculation, allowing the effects of adhesion molecules (ICAM-1) on cell mechanical properties to be observed while applying a mechanical deformation. The microrheology technique that tracks the thermal motion of granules within neutrophils was used to extract the local intracellular viscoelastic moduli. Small regional differences in rheology were found, with the central body region being significantly stiffer than the leading end cap region. When cells were exposed to ICAM-1, the regional differences were preserved, but the viscoelastic moduli were moderately increased in all regions. These results are consistent with the literature on leukocyte sequestration and provide insight into the regional rheological effects of deformation and adhesion molecules on neutrophils.

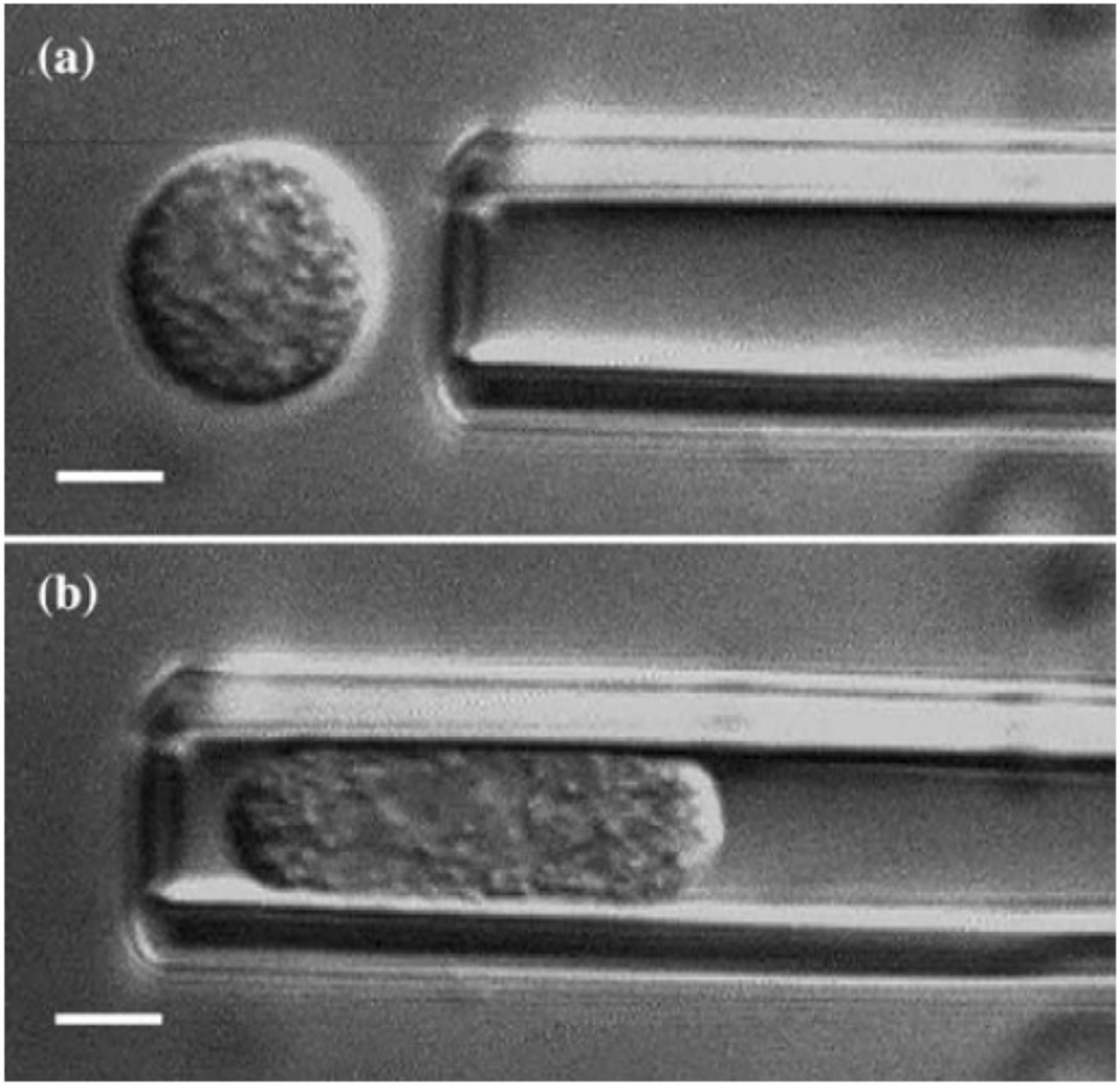


FIGURE 1. Neutrophil before (a) and after (b) aspiration into a capillary-sized micropipette. Scale bar = 5 μm.

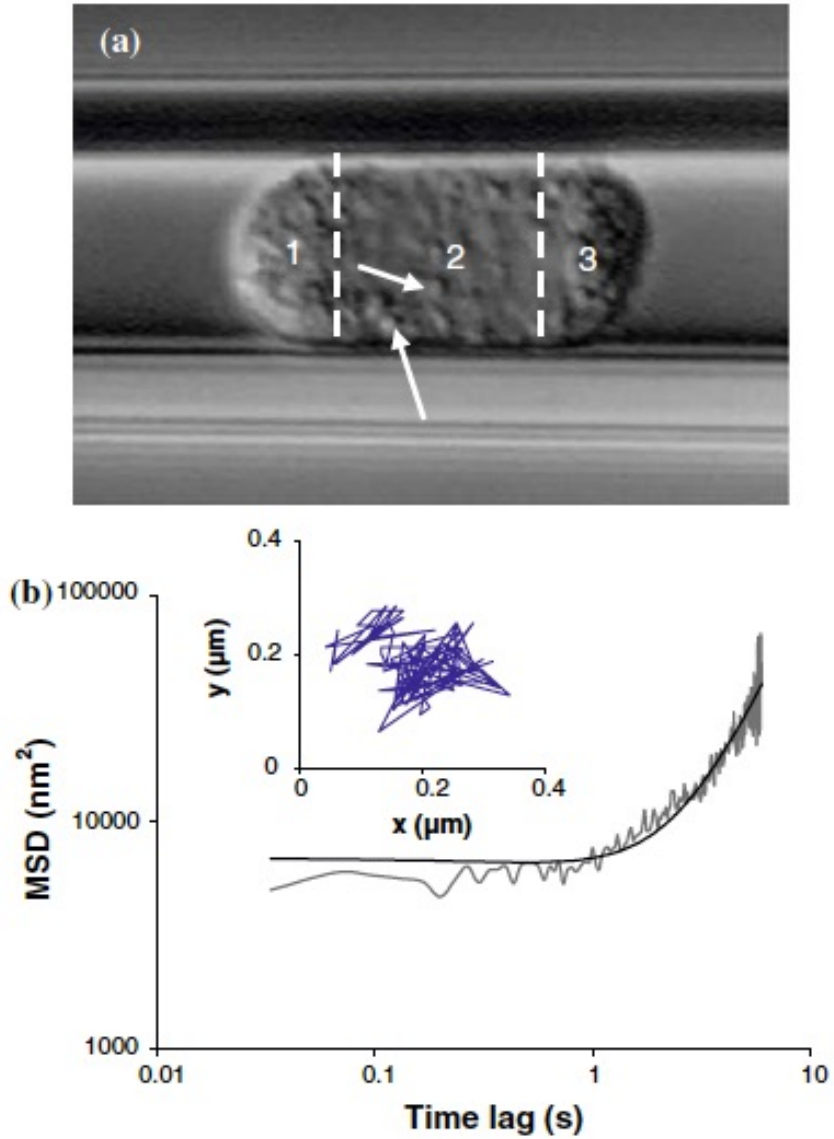


FIGURE 2. (a) DIC microscopy image of an aspirated neutrophil with regions identified: (1) trailing region; (2) body region; (3) leading region. The arrows point to potential granules that can be tracked. (b) Grey curve shows the mean square distribution vs. time lag for a sample particle. Black line shows polynomial fit. The Brownian motion of the particle is shown in the inset.

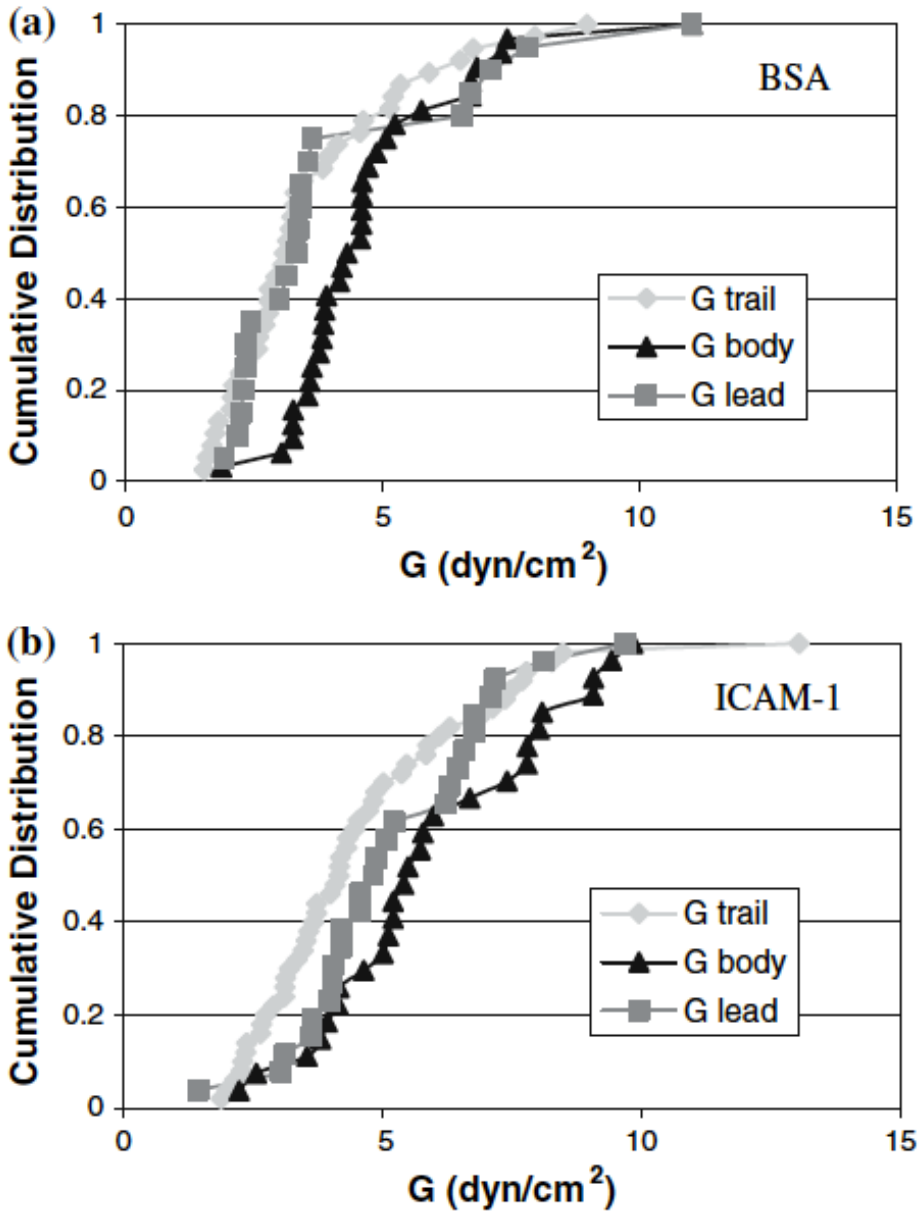


FIGURE 3. Cumulative probability distributions for stiffness *G* (in dyn/cm^2) for granules in different regions of neutrophils aspirated into (a) BSA-coated and (b) ICAM-1-coated micropipettes.

TABLE 1. Average mechanical properties for aspirated neutrophils.

Condition		$n_{granules}$	$\bar{G}$ (dyn/cm^2)	$\bar{G}'$ (dyn/cm^2)	$\bar{G}''$ (dyn·s/cm^2)	G''/G'
BSA	Trail	38	3.6 ± 0.3[a,c]	3.1 ± 0.2	1.7 ± 0.2	0.56 ± 0.08
	Body	32	4.8 ± 0.3[a,d]	4.0 ± 0.3	2.3 ± 0.3	0.58 ± 0.07
	Lead	20	4.1 ± 0.5[e]	3.3 ± 0.4	2.3 ± 0.4	0.70 ± 0.04
ICAM-1	Trail	50	4.6 ± 0.3[b,c]	3.9 ± 0.3	2.2 ± 0.2	0.55 ± 0.06
	Body	27	6.0 ± 1.1[b,d]	5.2 ± 1.0	2.7 ± 0.5	0.52 ± 0.14
	Lead	26	5.2 ± 1.0[e]	4.4 ± 0.8	2.4 ± 0.5	0.55 ± 0.15

[a, b, c, d, e]Pairs of symbols indicate that the two values are significantly different.

Q1: Algorithm of Successive Parabolic Interpolation.

If the scenario in the red box is true, which block of code is executed?

(a) If $x_{min} < x_1$ then
  (i) if $f(x_{min}) < f(x_1)$ choose x_0, x_{min}, x_1;
  (ii) if $f(x_{min}) > f(x_1)$ choose x_{min}, x_1, x_2.
(b) If $x_{min} > x_1$ then
  (i) if $f(x_{min}) < f(x_1)$ choose x_1, x_{min}, x_2;
  (ii) if $f(x_{min}) > f(x_1)$ choose x_0, x_1, x_{min}.

```
if xmin < x1
    if fxmin < fx1
        x2 = x1;
        fx2 = fx1;
        x1 = xmin;
        fx1 = fxmin;
    else
        x0 = xmin;
        fx0 = fxmin;
    end
else
    if fxmin < fx1
        x0 = x1;
        fx0 = fx1;
        x1 = xmin;
        fx1 = fxmin;
    else
        x2 = xmin;
        fx2 = fxmin;
    end
end
k = k + 1;
```

A

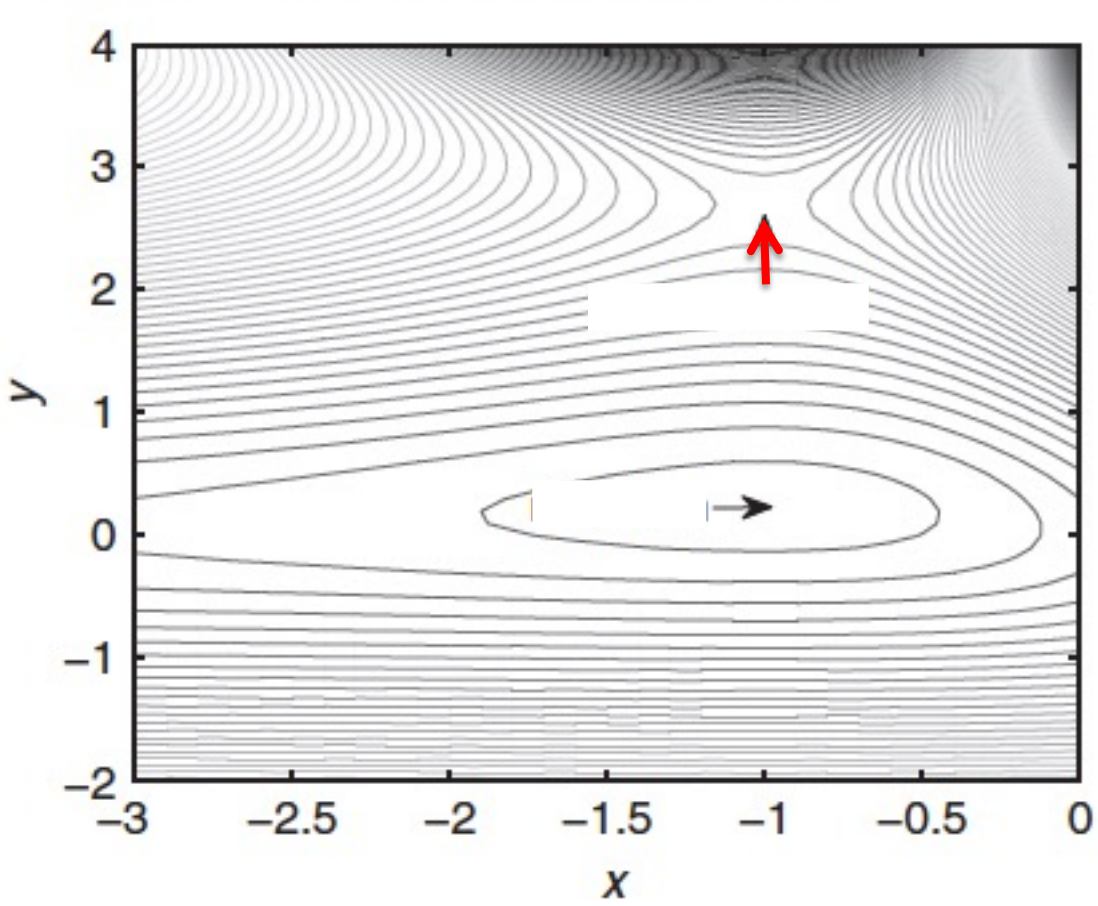
B

C

D

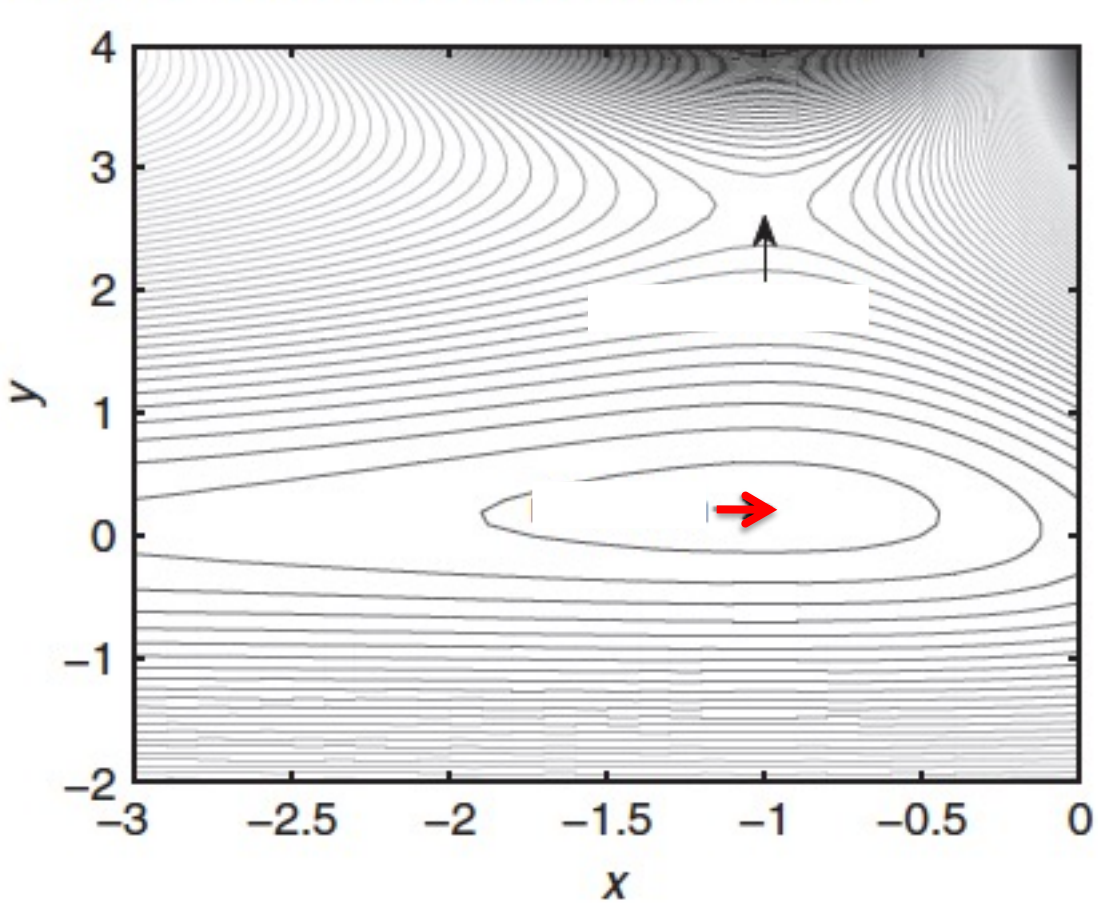
Q2: What type of critical point is indicated by the red arrow?

A. Minimum
B. Maximum
C. Saddle point
D. Inflection point
E. Can't tell



Q3: What type of critical point is indicated by the red arrow?

A. Minimum
B. Maximum
C. Saddle point
D. Inflection point
E. Can't tell



Q4: The method of steepest descent may converge on a local minimum, maximum, or saddle point, so after solving you must check to see which it is.

A. True
B. False

Weighted Linear Regression

- A final note on linear regression, let us examine the case where the variance of σ_b^2 is not constant!
- In this case we wish to weight the points in our regression analysis differently.
- This is weighted linear regression!
- Suppose we have the diagonal matrix Σ_b^2.
- The weighted problem is just…

Weighted Linear Regression

$$\min_{\mathbf{x}} (\mathbf{Ax} - \mathbf{b})^T (\Sigma_b^2)^{-1} (\mathbf{Ax} - \mathbf{b})$$

$$= \min_{\mathbf{x}} \mathbf{r}^T (\Sigma_b^2)^{-1} \mathbf{r}$$

where $(\Sigma_b^2)^{-1}$ is a diagonal matrix whose elements are just $1/\sigma^2_{bi}$.

- Thus we have weighted each point by the inverse of the variance of that point. This makes sense. Suppose the reason why σ_{bi} varied was that m_i points were averaged together to get b_i.

Weighted Linear Regression

- Okay, what is the formula for x?
- Just as before we take the gradient:

  (see the board…)

Undersampling and the Bootstrap

- Thus far we have considered error propagation/estimation techniques which rely on the regression formulas specific to linear regression.
- There are other numerical ways to estimate the error in the parameters, however, which apply to both linear and nonlinear regression.
- One approach is undersampling!

Undersampling and the Bootstrap

- Suppose we have a series of observations $b_i(t_i)$. We wish to fit this with a model:

  $$b_i \sim f(x,t_i)$$

  where f may be linear or nonlinear in x.
- If it's linear, we just use linear regression. If it's nonlinear, we still do regression, only now it's nonlinear regression.
- We want to estimate the error and covariance in x, e.g., we wish…

Undersampling and the Bootstrap

$$\Sigma_x^2 = E\{(\mathbf{x} - \boldsymbol{\mu}_\mathbf{x})(\mathbf{x} - \boldsymbol{\mu}_\mathbf{x})^T\}$$

- If the number of points N is fairly large, we can do this with undersampling.
- Suppose we take every m^{th} point. This gives us a set of N/m points from which we can calculate **x**. If we do this for the m independent sets of N/m points, we get m estimates for **x**!

Undersampling and the Bootstrap

- We can then get a sample covariance matrix:

$$\Sigma^2_{xixj} = 1/(m-1)\{\overline{x_i x_j} - \overline{x}_i \overline{x}_j\}$$

- Note that we did <u>not</u> require knowing the error in **b**! It also works equally well for linear and nonlinear regression.
- It's drawbacks are that it requires a pretty big N, and it requires multiple solutions for **x**. That can take a while for nonlinear problems.

Undersampling and the Bootstrap

- A similar approach is the bootstrap, which works pretty well with moderately sized data sets.
- Suppose we have, say, 20 observations $b_i(t_i)$. These observations are a subset of all possible observations.
- We can produce an approximation to this infinite set by periodically replicating our original data set!

Undersampling and the Bootstrap

- The idea is to then take samples of 20 observations from this replicated set and calculate **x**. We then compute $\Sigma_{\mathbf{x}}^2$ as before!
- This technique is appealing, but it only works if N is fairly large.
- This is because there is a non-zero probability of getting the same point $b_i(t_i)$ N times out of our replicated set, which leads to an ill-posed regression problem.

Undersampling and the Bootstrap

- Fortunately, this probably goes as

$$\sim (1/N)^{N-1}$$

which gets pretty small fairly fast.

(N=20 → P~10^{-25} !)

- The regression covariance is just:

$$\Sigma^2_{xixj} = 1/(p-1)\{\overline{x_i x_j} - \bar{x}_i \bar{x}_j\}$$

where we are solving the regression problem p times.

A final word on error and models

- As a final note on statistics, we have assumed throughout that the deviation between the observations and the model is random. This is, in general, **not true**!
- Thus, you tend to underestimate your error by ignoring the non-zero covariance in your data.
- It is important to always plot your residuals to see if there is a systematic deviation.
- A systematic deviation means that something is missing from your model and/or there is a systematic error in your data.
- Never forget that for large N, parametric error is dominated by systematic error!