

Monday, February 3

Modeling Nonlinearity

Four approaches to modeling a nonlinear relationship between the expected response and a quantitative explanatory variable.

1. polynomials
2. transformations
3. splines
4. nonlinear regression

The first three can be done with *linear models*.

Polynomial Regression

If we have a single explanatory variable x_i , then a *polynomial regression model* of degree k is

$$E(Y_i) = \beta_0 + \beta_1 x_i + \beta_2 x_i^2 + \cdots + \beta_k x_i^k.$$

Note that this *is* a linear *model* since we can write it as

$$E(Y_i) = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + \cdots + \beta_k x_{ik},$$

where $x_{i1} = x_i, x_{i2} = x_i^2, \dots, x_{ik} = x_i^k$.

Example: Consider again the `ToothGrowth` data but with dose treated as a quantitative explanatory variable, and ignoring supplement type for now. Note the use of the “inhibit” function `I` here.

```
m <- lm(len ~ dose + I(dose^2), data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	-2.49	3.178	-0.7836	4.365e-01
dose	30.16	6.147	4.9052	8.148e-06
I(dose^2)	-7.93	2.366	-3.3514	1.432e-03

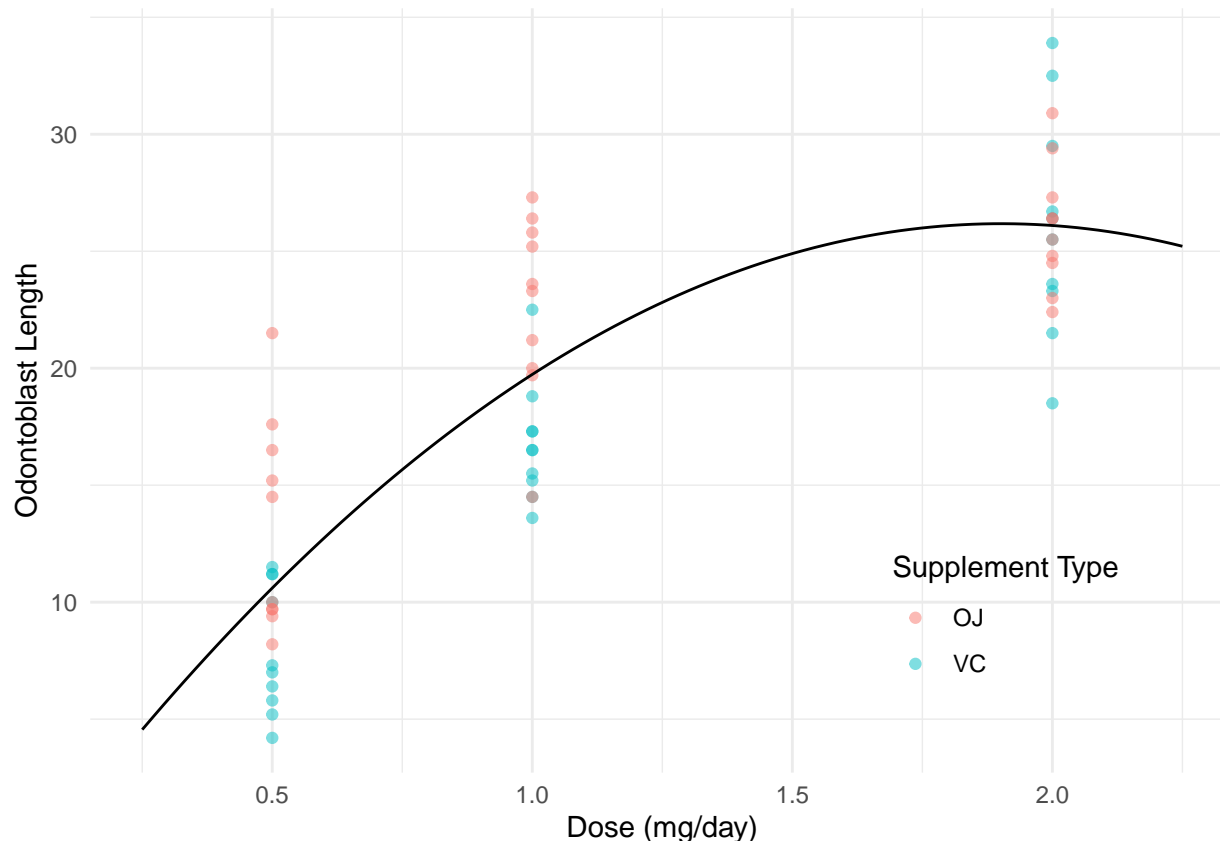
This model is

$$E(L_i) = \beta_0 + \beta_1 d_i + \beta_2 d_i^2,$$

where d_i is dose.

```
d <- expand.grid(dose = seq(0.25, 2.25, length = 100))
d$yhat <- predict(m, newdata = d)

p <- ggplot(ToothGrowth, aes(x = dose, y = len)) +
  geom_point(aes(color = supp), alpha = 0.5) +
  geom_line(aes(y = yhat), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") +
  theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



Note that the following are equivalent ways to specify this model.

```
# create a new variable for squared dose
ToothGrowth$dose2 <- ToothGrowth$dose^2
m <- lm(len ~ dose + dose2, data = ToothGrowth)

# specify squared dose in the model formula using the "inhibit" function
m <- lm(len ~ dose + I(dose^2), data = ToothGrowth)

# use the poly function to create the extra term
m <- lm(len ~ poly(dose, degree = 2), data = ToothGrowth)
```

I recommend not using the first approach of creating a new variable only because it is easier to have the transformation “built in” to the model when applying other functions to the model object like `predict` or `contrast`.

Note: Using `poly` without the option `raw = TRUE` will produce “orthogonal polynomials” which is a re-parameterization of the model. This approach is sometimes recommended due to numerical instability of “raw” polynomials, but in many cases this is not an issue. But the `poly` function is sometimes convenient, especially for polynomials of higher degree.

Clearly in such a model the rate of change in expected length is *not* necessarily constant.

```
library(trtools)
contrast(m, a = list(dose = 1), b = list(dose = 0.5)) # 0.5 to 1
```

estimate	se	lower	upper	tvalue	df	pvalue
9.13	1.341	6.444	11.82	6.806	57	6.697e-09

```
contrast(m, a = list(dose = 1.5), b = list(dose = 1)) # 1 to 1.5
```

```
estimate      se lower upper tvalue df    pvalue
  5.165 0.4472  4.27  6.06  11.55 57 1.47e-16
```

This can also be seen mathematically by writing the model as

$$E(L_i) = \beta_0 + \beta_1 x_i + \beta_2 x_i^2 = \beta_0 + \underbrace{(\beta_1 + \beta_2 x_i)}_{\delta_i} x_i = \beta_0 + \delta_i x_i,$$

so that the rate of change in length per unit increase in dose *depends on dose* (if $\beta_2 \neq 0$). In a sense, dose is “interacting with itself” — i.e., the “effect” of a one unit increase in dose depends on the dose.

We can have the polynomial depend on (i.e, interact with) supplement type.

```
m <- lm(len ~ dose + I(dose^2) + supp + dose:supp + I(dose^2):supp, data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	-1.433	3.847	-0.3726	7.109e-01
dose	34.520	7.442	4.6384	2.272e-05
I(dose^2)	-10.387	2.864	-3.6260	6.383e-04
suppVC	-2.113	5.440	-0.3885	6.992e-01
dose:suppVC	-8.730	10.525	-0.8295	4.105e-01
I(dose^2):suppVC	4.913	4.051	1.2129	2.305e-01

Note that we could also have written

```
m <- lm(len ~ poly(dose, 2)*supp, data = ToothGrowth)
```

In a model formula argument, $a*b$ expands to $a + b + a:b$.

This model can be written as

$$E(L_i) = \begin{cases} \beta_0 + \beta_1 d_i + \beta_2 d_i^2, & \text{if supplement type is OJ,} \\ \beta_0 + \beta_3 + (\beta_1 + \beta_4) d_i + (\beta_2 + \beta_5) d_i^2, & \text{if supplement type is VC,} \end{cases}$$

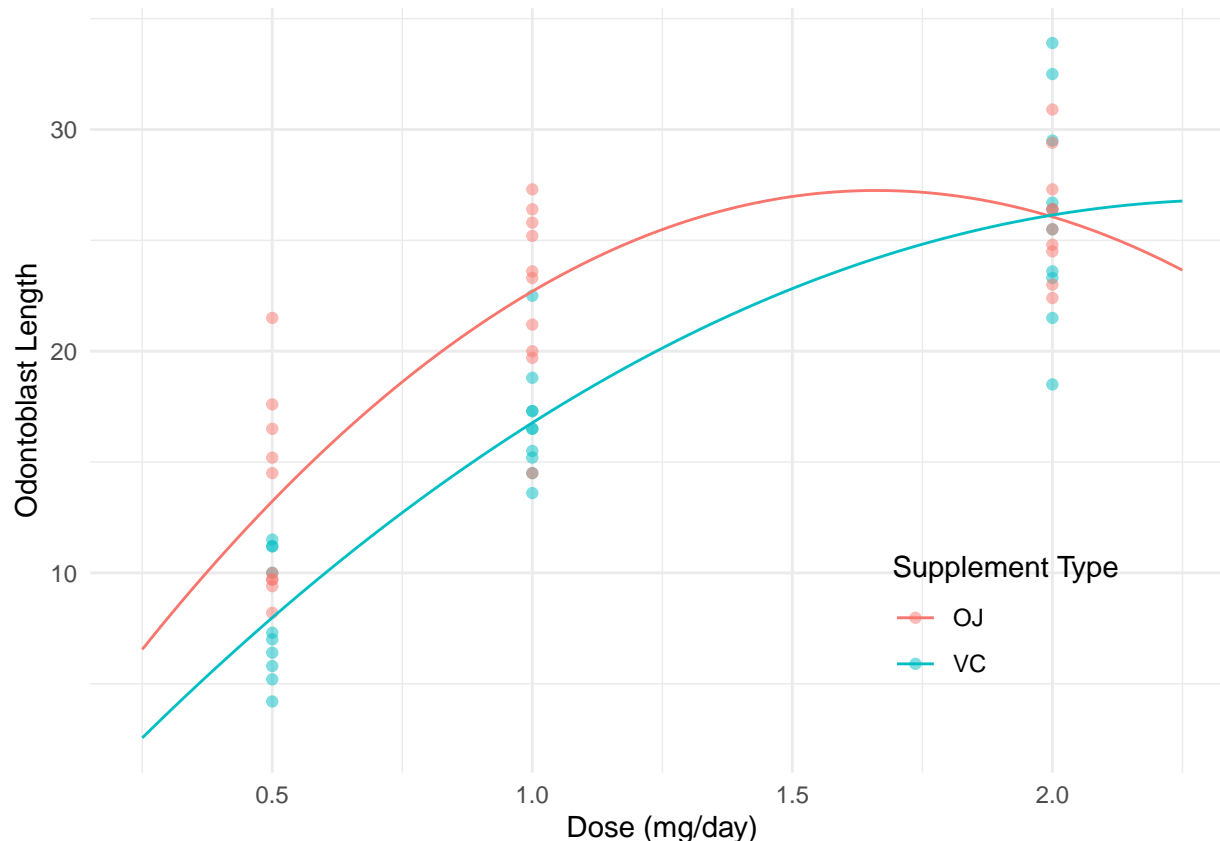
where d_i is dose, or alternatively as

$$E(L_i) = \begin{cases} \beta_0 + \beta_1 d_i + \beta_2 d_i^2, & \text{if supplement type is OJ,} \\ \gamma_0 + \gamma_1 d_i + \gamma_2 d_i^2, & \text{if supplement type is VC,} \end{cases}$$

where $\gamma_0 = \beta_0 + \beta_3$, $\gamma_1 = \beta_1 + \beta_4$, and $\gamma_2 = \beta_2 + \beta_5$. There is a distinct polynomial of degree two for each supplement type.

```
d <- expand.grid(supp = c("OJ", "VC"), dose = seq(0.25, 2.25, length = 100))
d$yhat <- predict(m, newdata = d)
```

```
p <- ggplot(ToothGrowth, aes(x = dose, y = len, color = supp)) +
  geom_point(alpha = 0.5) + geom_line(aes(y = yhat), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") + theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



Polynomials are, in principle, quite general. But in many cases we would like to have a monotonic relationship, and/or have a model exhibit an asymptote. Finally, the parameters of a polynomial model are not easily to interpret.

Logarithmic Transformations

Applying a *logarithmic transformation* to an explanatory variable may be useful for explanatory variables that tend to have “diminishing returns” with respect to the expected response.

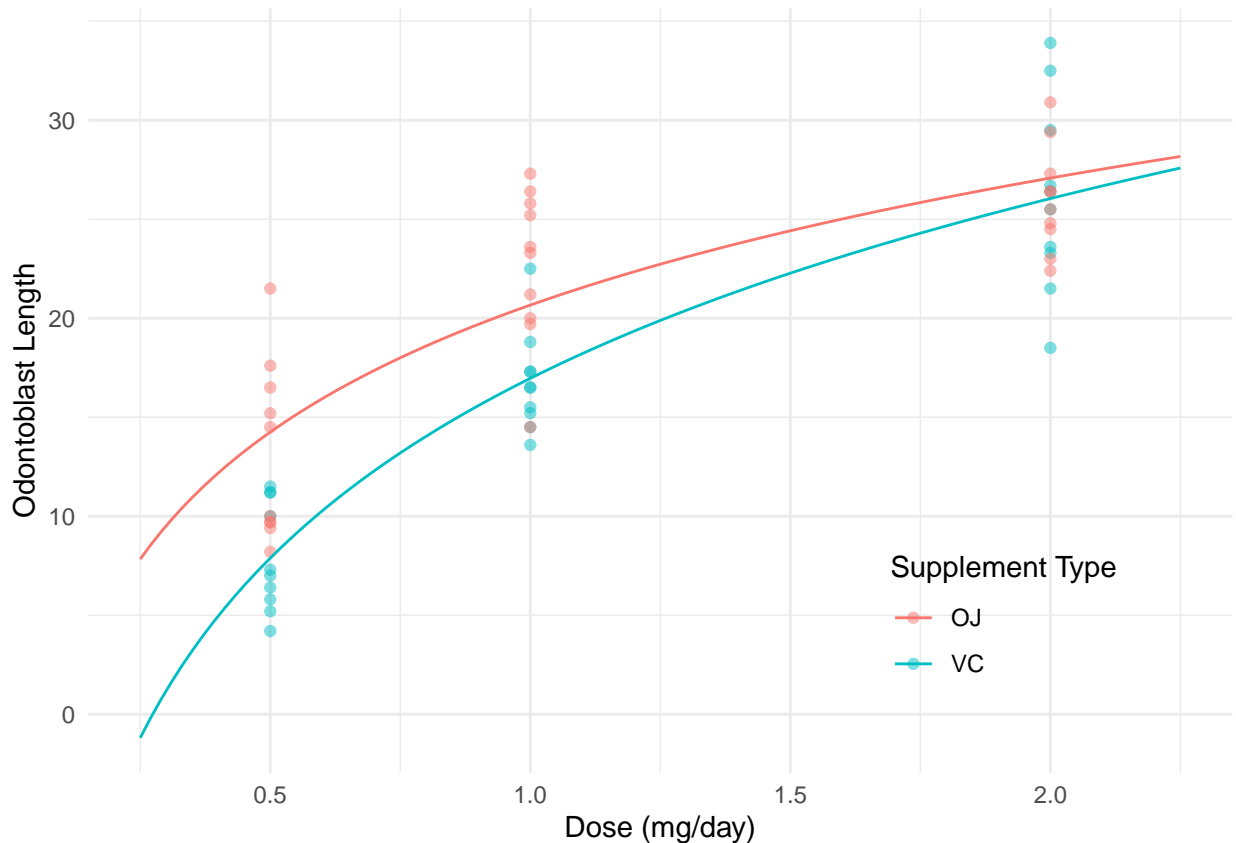
Example: Consider a linear model for expected length but now with $\log(\text{dose})$ as the explanatory variable.

```
m <- lm(len ~ log(dose) + supp + log(dose):supp, data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	20.663	0.6791	30.425	1.629e-36
log(dose)	9.255	1.2000	7.712	2.303e-10
suppVC	-3.700	0.9605	-3.852	3.033e-04
log(dose):suppVC	3.845	1.6971	2.266	2.737e-02

```
d <- expand.grid(supp = c("OJ", "VC"), dose = seq(0.25, 2.25, length = 100))
d$yhat <- predict(m, newdata = d)
```

```
p <- ggplot(ToothGrowth, aes(x = dose, y = len, color = supp)) +
  geom_point(alpha = 0.5) + geom_line(aes(y = yhat), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") + theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



Note that \log is the “natural” logarithm or base- e logarithm sometimes written as $\ln(x)$ or $\log_e(x)$. Here are few things to remember about logarithms when using them for transformations of explanatory variables.

1. Logarithms of different bases are *proportional*. In general

$$\log_b(x) = c \log_a(x),$$

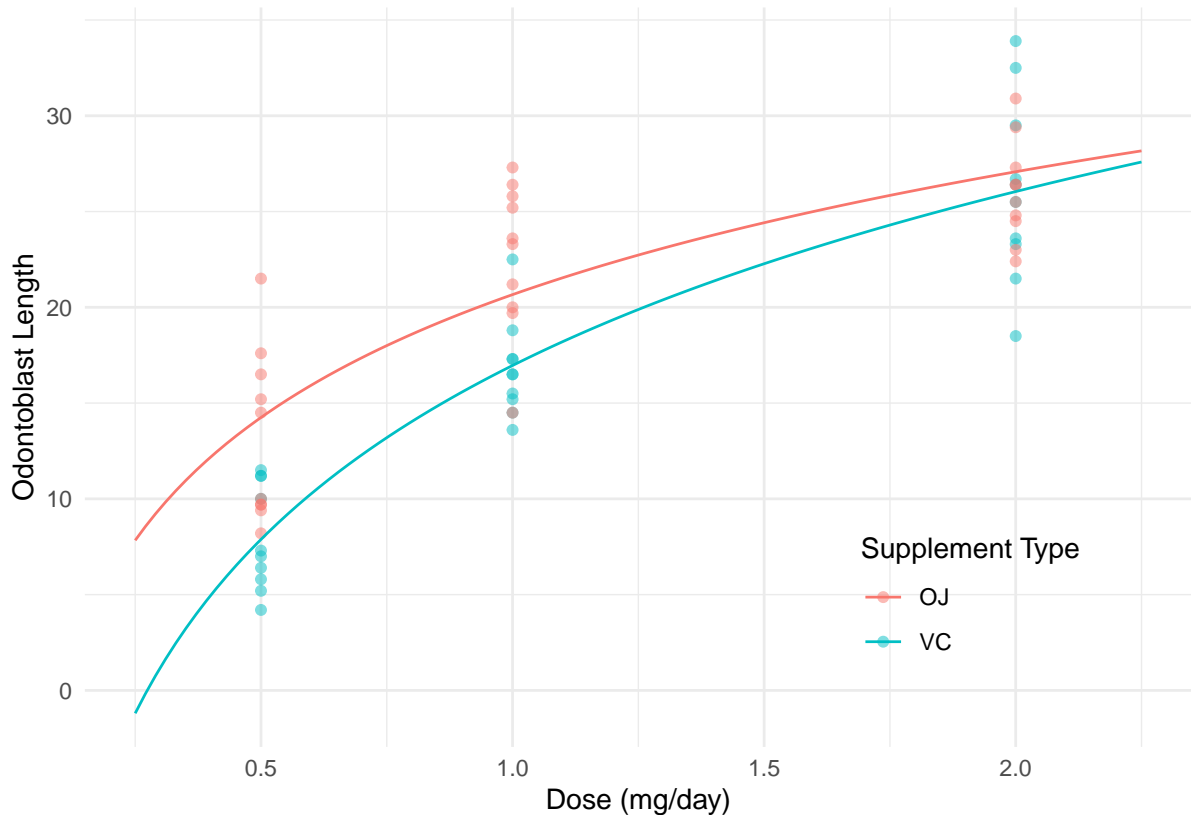
where $c = 1/\log_a(b)$. So usually when we are using things like `contrast` or the `emmeans` package to facilitate our inferences the base does not matter. You can use `log2` for $\log_2(x)$ and `log10` for $\log_{10}(x)$, and for an arbitrary base b you can use `log(x,b)` for $\log_b(x)$.

```
m <- lm(len ~ log2(dose) + supp + log2(dose):supp, data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	20.663	0.6791	30.425	1.629e-36
log2(dose)	6.415	0.8318	7.712	2.303e-10
suppVC	-3.700	0.9605	-3.852	3.033e-04
log2(dose):suppVC	2.665	1.1763	2.266	2.737e-02

```
d <- expand.grid(supp = c("OJ", "VC"), dose = seq(0.25, 2.25, length = 100))
d$yhat <- predict(m, newdata = d)
```

```
p <- ggplot(ToothGrowth, aes(x = dose, y = len, color = supp)) +
  geom_point(alpha = 0.5) + geom_line(aes(y = yhat), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") + theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



2. If we apply a log transformation to x , then the effect of increasing/decreasing x by some amount is not constant, but the effect of increasing/decreasing x by a *factor* is constant. For example, suppose we have the model

$$E(Y) = \beta_0 + \beta_1 \log(x).$$

Then for any $c > 0$ then

$$\beta_0 + \beta_1 \log(cx) = \beta_0 + \beta_1 \log(c) + \beta_1 \log(x) = E(Y) + \beta_1 \log(c)$$

so then $E(Y)$ increases/decreases by $\beta_1 \log(c)$. For example, the effect of *doubling* of *halving* dose is constant in this model.

```
contrast(m,
  a = list(dose = 1, supp = c("OJ","VC")),
  b = list(dose = 0.5, supp = c("OJ","VC")),
  cnames = c("OJ", "VC"))
```

	estimate	se	lower	upper	tvalue	df	pvalue
OJ	6.415	0.8318	4.749	8.081	7.712	56	2.303e-10
VC	9.080	0.8318	7.414	10.746	10.916	56	1.733e-15

```
contrast(m,
  a = list(dose = 2, supp = c("OJ","VC")),
  b = list(dose = 1, supp = c("OJ","VC")),
  cnames = c("OJ", "VC"))
```

	estimate	se	lower	upper	tvalue	df	pvalue
OJ	6.415	0.8318	4.749	8.081	7.712	56	2.303e-10
VC	9.080	0.8318	7.414	10.746	10.916	56	1.733e-15

3. Recall that $\log(x)$ is only defined for $x > 0$.

Exponential Transformations

Consider the linear model

$$E(Y) = \beta_0 + \beta_1 2^{-x/h}$$

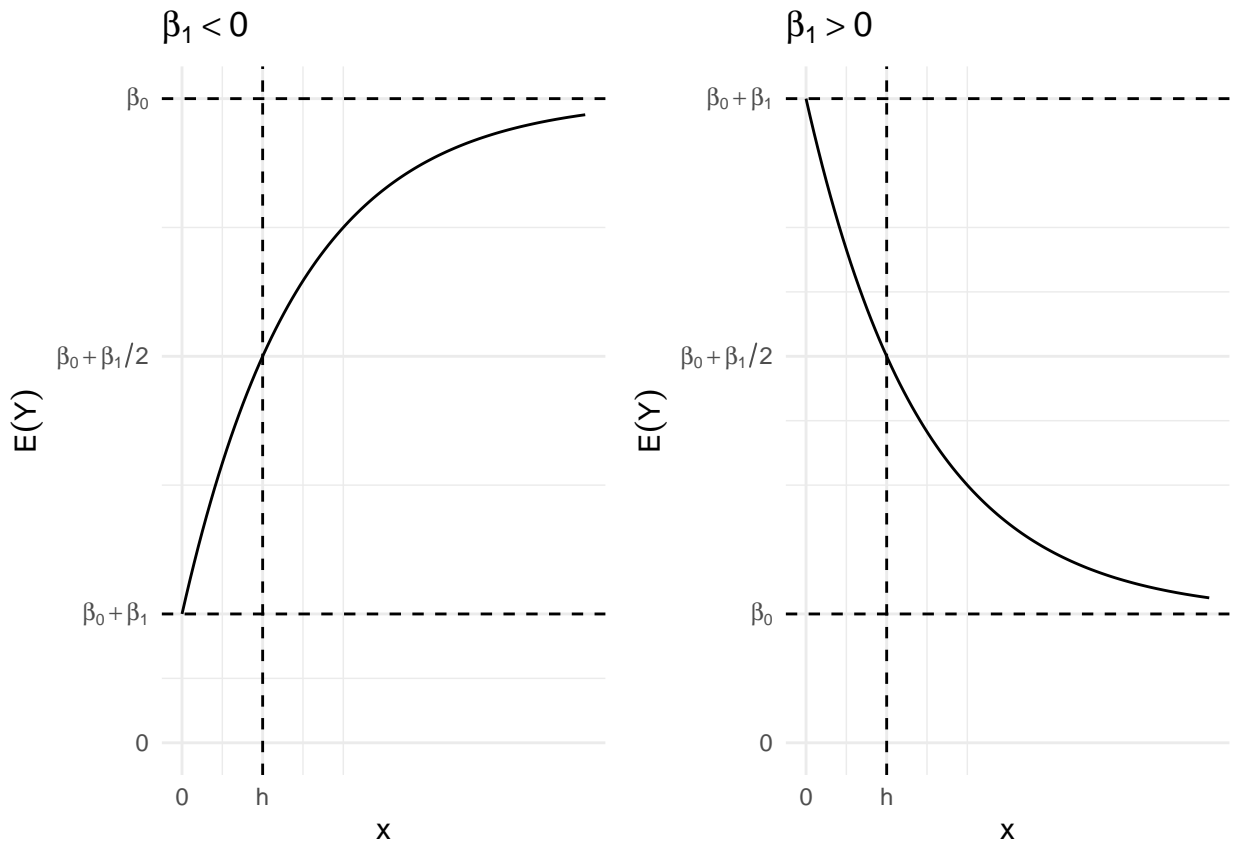
where $h > 0$ is some specified value. This applies an *exponential* transformation to x with the following properties.

1. If $x = 0$ then $E(Y) = \beta_0 + \beta_1$, so the “ y -intercept” is $\beta_0 + \beta_1$.
2. As x increases then $E(Y)$ approaches an asymptote of β_0 . This is an *upper* (if $\beta_1 < 0$) or *lower* (if $\beta_1 > 0$) asymptote.¹
3. The quantity h can be interpreted as the “half-life” of the curve in the sense that it is the value of x at which the expected responses is half way between the intercept at $\beta_0 + \beta_1$ and its upper/lower asymptote at β_0 because if $x = h$ then

$$E(Y) = \beta_0 + \beta_1 2^{-x/h} = \beta_0 + \beta_1/2,$$

and $\beta_0 + \beta_1/2$ is the midpoint between the “intercept” of $E(Y) = \beta_0 + \beta_1$ and the asymptote of β_0 .

4. If $\beta_1 < 0$ then $-\beta_1$ is how much $E(Y)$ *increases* from $x = 0$ as it approaches the asymptote, while if $\beta_1 > 0$ then β_1 is how much $E(Y)$ *decreases* from when $x = 0$ as it approaches the asymptote.



Consider again a linear model for the `ToothGrowth` data with an exponential transformation of dose with $h = 1$.

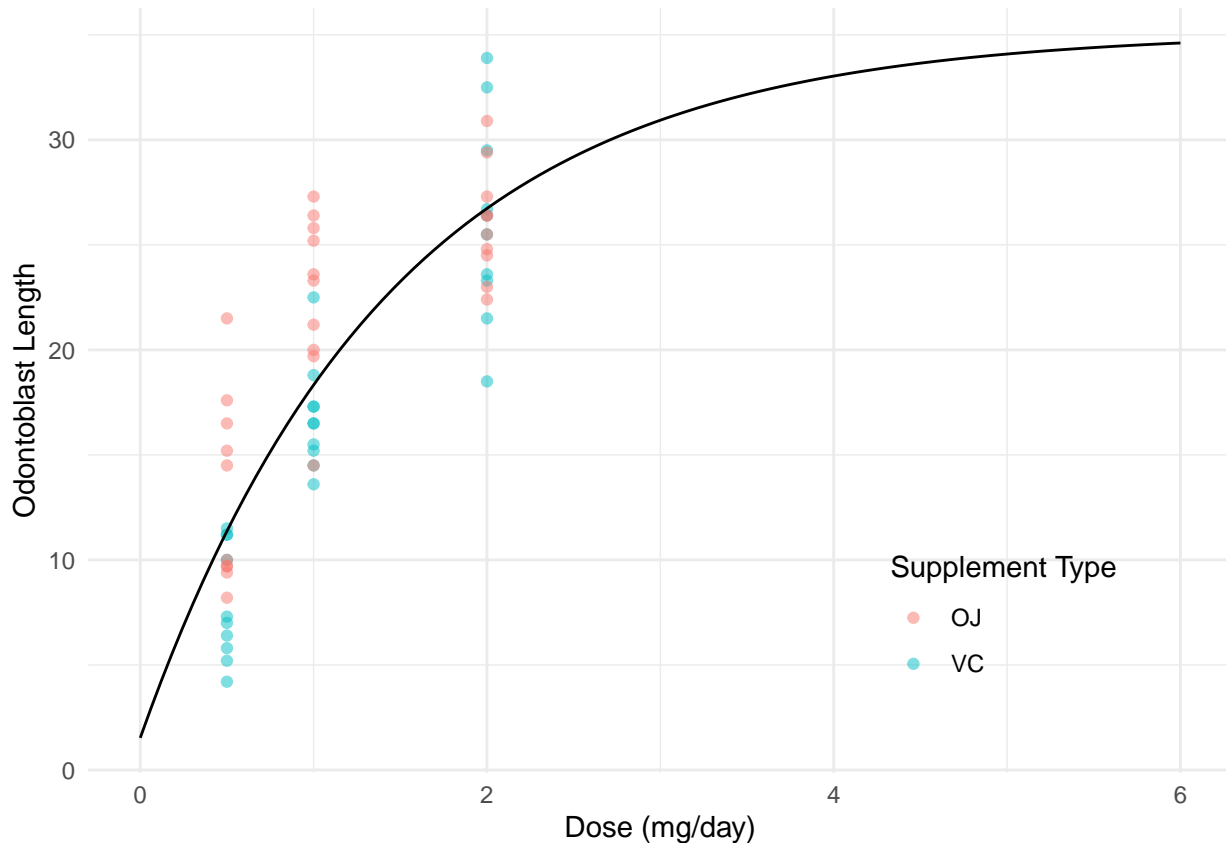
¹This can be seen by showing that $\lim_{x \rightarrow \infty} \beta_0 + \beta_1 2^{-x/h} = \beta_0$ if $h > 0$, and by showing that the first derivative of $\beta_0 + \beta_1 2^{-x/h}$ with respect to x is positive if $\beta_1 < 0$ and negative if $\beta_1 > 0$ if $h > 0$.

```
m <- lm(len ~ I(2^(-dose/1)), data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	35.14	1.555	22.60	1.942e-30
I(2^(-dose/1))	-33.61	2.988	-11.25	3.303e-16

```
d <- expand.grid(supp = c("OJ", "VC"), dose = seq(0, 6, length = 100))
d$yhat <- predict(m, newdata = d)
```

```
p <- ggplot(ToothGrowth, aes(x = dose, y = len, color = supp)) +
  geom_point(alpha = 0.5) + xlim(0,6) +
  geom_line(aes(y = yhat), color = "black", data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") + theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



```
lincon(m, a = c(1,1)) # intercept
```

	estimate	se	lower	upper	tvalue	df	pvalue
(1,1),0	1.528	1.635	-1.745	4.8	0.9345	58	0.3539

Now suppose that we let the effect of dose “interact” with supplement type.

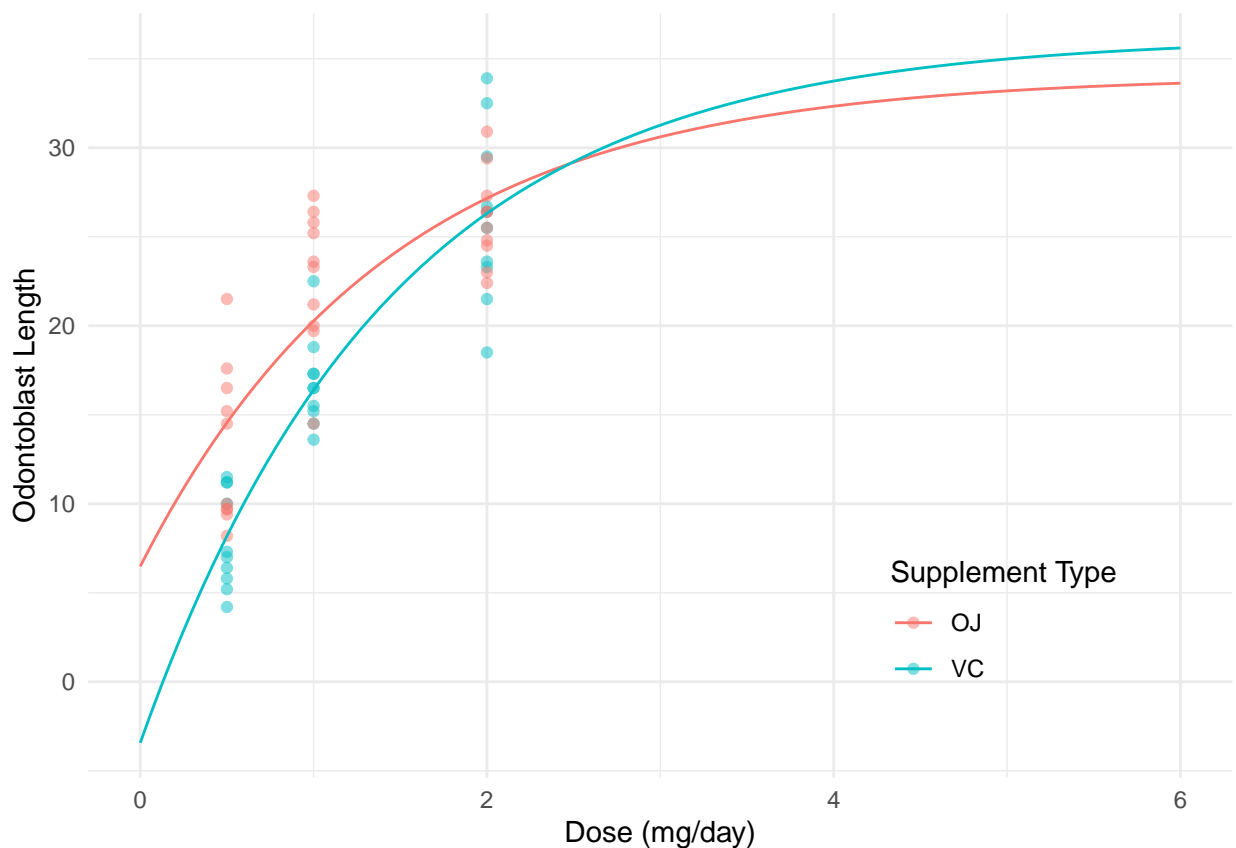
```
m <- lm(len ~ I(2^(-dose/1)) + supp + supp:I(2^(-dose/1)), data = ToothGrowth)
summary(m)$coefficients
```

	Estimate	Std. Error	t value	Pr(> t)
--	----------	------------	---------	----------


```
(Intercept)          34.054          1.925 17.6872 1.375e-24
I(2^(-dose/1))      -27.569          3.700 -7.4519 6.199e-10
suppVC              2.169           2.723  0.7964 4.291e-01
I(2^(-dose/1)):suppVC -12.083          5.232 -2.3094 2.463e-02
```

```
d <- expand.grid(supp = c("OJ", "VC"), dose = seq(0, 6, length = 100))
d$yhat <- predict(m, newdata = d)
```

```
p <- ggplot(ToothGrowth, aes(x = dose, y = len, color = supp)) +
  geom_point(alpha = 0.5) + xlim(0,6) +
  geom_line(aes(y = yhat), data = d) +
  labs(x = "Dose (mg/day)", y = "Odontoblast Length",
       color = "Supplement Type") + theme_minimal() +
  theme(legend.position = "inside", legend.position.inside = c(0.8,0.2))
plot(p)
```



This model can be written as

$$E(Y_i) = \beta_0 + \beta_1 2^{-x_i/h} + \beta_2 d_i + \beta_3 d_i 2^{-x_i/h},$$

where $d_i = 1$ if the supplement type is VC, and $d_i = 0$ otherwise, and $h = 1$. We can also write this model case-wise as

$$E(Y_i) = \begin{cases} \beta_0 + \beta_1 2^{-x_i/h}, & \text{if the supplement type of the } i\text{-th observation is OJ,} \\ \beta_0 + \beta_2 + (\beta_1 + \beta_3) 2^{-x_i/h}, & \text{if the supplement type of the } i\text{-th observation is VC,} \end{cases}$$

or

$$E(Y_i) = \begin{cases} \beta_0 + \beta_1 2^{-x_i/h}, & \text{if the supplement type of the } i\text{-th observation is OJ,} \\ \gamma_0 + \gamma_1 2^{-x_i/h}, & \text{if the supplement type of the } i\text{-th observation is VC,} \end{cases}$$

where $\gamma_0 = \beta_0 + \beta_2$ and $\gamma_1 = \beta_1 + \beta_3$. We can make inferences for the intercepts and asymptotes for *each* supplement type using `lincon`.

```
lincon(m, a = c(1,1,0,0)) # b0 + b1 = intercept for OJ
```

	estimate	se	lower	upper	tvalue	df	pvalue
(1,1,0,0),0	6.485	2.024	2.429	10.54	3.203	56	0.002243

```
lincon(m, a = c(1,1,1,1)) # g0 + g1 = b0 + b2 + b1 + b3 = intercept for VC
```

	estimate	se	lower	upper	tvalue	df	pvalue
(1,1,1,1),0	-3.429	2.024	-7.485	0.6261	-1.694	56	0.09582

```
lincon(m, a = c(1,0,1,0)) # g0 = b0 + b2 = asymptote for VC
```

	estimate	se	lower	upper	tvalue	df	pvalue
(1,0,1,0),0	36.22	1.925	32.37	40.08	18.81	56	7.07e-26

We can also obtain (approximate) inferences using `contrast`.

```
contrast(m, a = list(dose = 0, supp = c("OJ", "VC")),
         cname = c("OJ intercept", "VC intercept"))
```

	estimate	se	lower	upper	tvalue	df	pvalue
OJ intercept	6.485	2.024	2.429	10.5401	3.203	56	0.002243
VC intercept	-3.429	2.024	-7.485	0.6261	-1.694	56	0.095824

```
contrast(m, a = list(dose = 100, supp = c("OJ", "VC")),
         cname = c("OJ asymptote", "VC asymptote"))
```

	estimate	se	lower	upper	tvalue	df	pvalue
OJ asymptote	34.05	1.925	30.20	37.91	17.69	56	1.375e-24
VC asymptote	36.22	1.925	32.37	40.08	18.81	56	7.070e-26

But wouldn't it make sense to have something like the following?

$$E(Y_i) = \begin{cases} \beta_0 + \beta_1 2^{-x_i/h_{OJ}}, & \text{if the supplement type of the } i\text{-th observation is OJ,} \\ \beta_0 + \beta_1 2^{-x_i/h_{VC}}, & \text{if the supplement type of the } i\text{-th observation is VC,} \end{cases}$$

because at $x = 0$ and as $x \rightarrow \infty$ there should be no difference in the supplement type, but there might be a difference in how “fast” the expected response increases with dose. But unless we *know* h_{OJ} and h_{VC} , this model would be *nonlinear* (i.e., the model is not linear if h_{OJ} and h_{VC} are *unknown parameters* as opposed to known values).