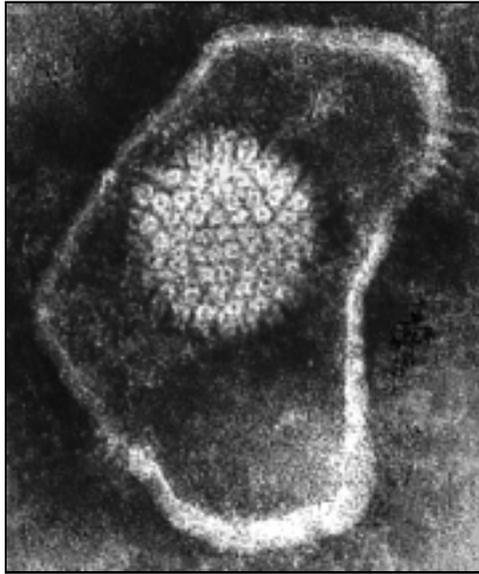Figure 1: Electron micrograph of an HSV-1 capsid. (The capsid is the round structure in the center.)

Herpes[1] is (perhaps) the most notorious of the common viral infections that afflict humans, with large amounts of late-night humor[2] devoted to the disease and its uncomfortable symptoms. The two viruses behind these ribald jokes are the herpes simplex virus 1 and 2 (HSV-1 and HSV-2). Figure 1[3] shows an electron micrograph of an HSV-1 capsid[4]. The diameter of the capsid shown in Figure 1 is about 0.0000001 meters.

Figure 2: Oral lesions on the lips and near the mouth. These outbreaks are normally the result of HSV-1 infection, although not all individuals who are infected with HSV-1 show symptoms.

Perhaps the most familiar (and most easily recognized) signs of HSV-1 infection are the highly infectious sores that occasionally appear on the skin of some people who are infected with HSV (see Figure 2[5]). Although lesions are most common around the nose, mouth and eyes they may also

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[1] Technically, "herpes" is not a single virus, but actually a family including more than 80 distinct (but related) viruses. Eight of these viruses are known to cause disease in humans, with the most common being the lesions (cold sores) caused by the Herpes Simplex Viruses, HSV-1 and HSV-2, and chicken pox.

[2] The late-night humor is generally devoted to genital herpes. This is caused by a virus that is usually referred to as HSV-2 (for Herpes Simplex Virus 2). HSV-1 (the virus that usually causes cold sores and other oral lesions) and HSV-2 appear identical when examined with an electron microscope. Although HSV-1 can cause genital herpes and HSV-2 can cause oral herpes (cold sores) HSV-1 infections are more common above the waist and HSV-2 infections are more common below the waist, for reasons that are still not clear to scientists.

[3] Image source: http://www.med.sc.edu:85/

[4] A *capsid* is the protective shell of proteins that surrounds the genetic material of the virus.
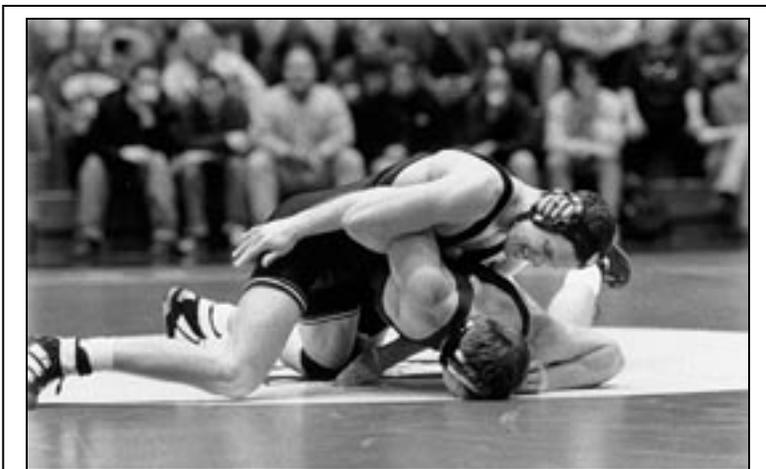
[5] Image source: http://www.dent.ucla.edu/

Figure 3: Amateur wresting involves a very high degree of direct skin-to-skin contact between competitors.

appear on other sites around the body, including the head, arms and torso. HSV-1 is usually transmitted by skin-to-skin contact with an individual who has infectious lesions on his or her body[6]. Athletes who participate in sports that involve a lot of skin-to-skin contact (such as amateur wrestling, see Figure 3[7]) are at a particularly high risk of contracting HSV-1 from infectious competitors. In fact, HSV-1 infections are so common among athletes like amateur wrestlers that in this context the infection is given its own name: herpes gladiatorum. In addition to producing painful blisters and lesions (cold sores) infection with herpes gladiatorum may also result in eye infections such as conjunctivitis (pink eye) as well as constitutional symptoms such as fever, chills, sore throat and headache.

In 1989, a group of medical researchers studies an outbreak of herpes gladiatorum among a group of teenage boys who participated in a summer camp for amateur wrestlers in Minnesota. The results of this investigation were reported in the prestigious New England Journal of Medicine:

- E. A. Belongia, J. L. Goodman, E. J. Holland, C. W. Anres, S. R. Homann, R. L. Mahanti, M. W. Mizener, A. Erice and M. T. Osterholm. (1991) "An outbreak of herpes gladiatorum at a high-school wrestling camp." *New England Journal of Medicine*, **325**(13): 906-910.

In this ICE, you will examine some of the mathematical models that the researchers developed to describe the spread of the disease.

- A total of 175 boys attended the wrestling camp. Let t represent the length of time (in days) that the camp had been running, and $P(t)$ represent the number of boys who were infected with herpes gladiatorum. Under what conditions would you expect the value of $P(t)$ to be constant? (Assume that the boys only had skin-to-skin contact with other boys in the camp.)

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[6] Sources: T. M. Becker (1992) "Herpes gladiatorum: a growing problem in sports medicine." *Cutis*, **50**: 150-152, and B. B. Adams (2001) "Which skin infections are transmitted between athletes?" *British Journal of Sports Medicine*, **34**: 413-414.

[7] Image source: http://www.niu.edu/athletics/wrestling/

- **Under what conditions would you expect the derivative** $P'(t)$ **to be equal to zero?**

Although the exact number of boys who exhibited infectious lesions at the beginning of the camp was unknown, the researchers identified four distinct strains of HSV-1, suggesting that at the beginning of the camp ($t = 0$) at least four boys were spreading HSV-1 to the others.

- **Using the axes provided below, sketch a possible graph showing** $P(t)$ **versus** t**. (Note that there is not a "right answer" that we are looking for here - it is more the overall shape of the graph that we are interested in.)**

*Number of boys with HSV-1* (y-axis: 0, 50, 100, 150, 200) — *Time* (x-axis)
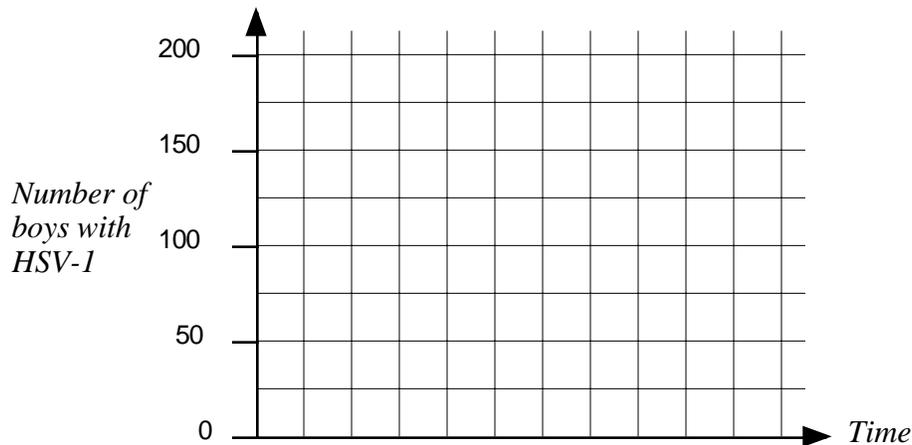
- **Which of the following differential equations seems to be compatible with the information that you have about** $P(t)$ **so far? What specific features of the differential equations are you looking for?**

- $P'(t) = -0.000637 \cdot P(t)$

- $P'(t) = -0.000637 \cdot \left[P(t) - 175\right]$

- $P'(t) = +0.000637 \cdot P(t) \cdot \left[P(t) - 175\right]$

- $P'(t) = -0.000637 \cdot P(t) \cdot \left[P(t) - 175\right]$

The slope field for the equation: $P'(t) = -0.000637 \cdot P(t) \cdot \left[P(t) - 175\right]$
is shown below.
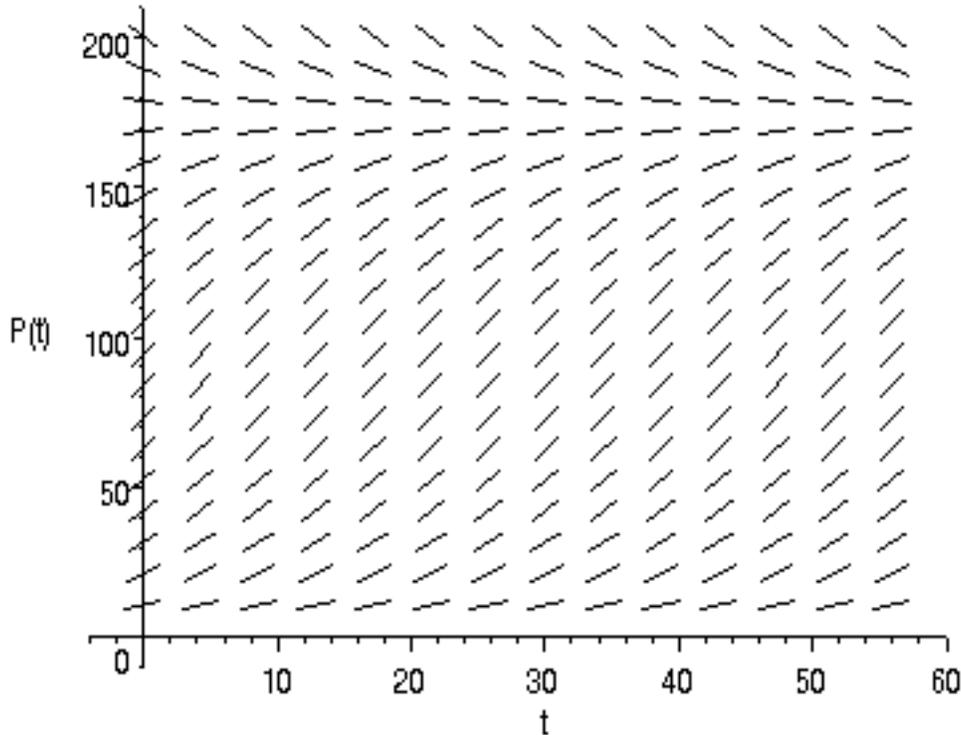
The camp that the researchers studied was only four weeks (28 days) long. By the end of the camp, 60 boys showed symptoms of HSV-1 infection[8]. In this last part of the ICE, you will investigate what might have happened if the camp had gone on longer, or if the researchers had studied a situation where the wrestlers trained together for a longer period of time.

• Using the slope field and what you know about the number of infected boys at $t = 0$ and $t = 28$, sketch as accurate a graph of $P(t)$ as you possibly can.

• Assume that the group of wrestlers continued to train together for longer than just four weeks. About when would have 150 boys been infected with herpes gladiatorum?

• Assume that the group of wrestlers continued to train together for longer than just four weeks. About when (in terms of time and in terms of number of boys infected) would the herpes gladiatorum have been spreading the fastest through the group of wrestlers?

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[8] Source: E. A. Belongia, et.al. (1991) "An outbreak of herpes gladiatorum at a high-school wrestling camp." *New England Journal of Medicine*, **325**(13): 906-910.

Equation for Derivative	Equilibrium solution(s)	Appearance of Slope field	Nature of Equilibrium solution(s)
$y'(t) = y(t) - 2$	• y(t) = 2		y(t) = 2 is an unstable equilibrium
$y'(t) = y(t) \cdot [y(t) - 2]$	• y(t) = 0 • y(t) = 2		y(t) = 0 is a stable equilibrium y(t) = 2 is an unstable equilibrium
$y'(t) = [y(t) - 2]^2$	• y(t) = 2		y(t) = 2 is a semi-stable equilibrium