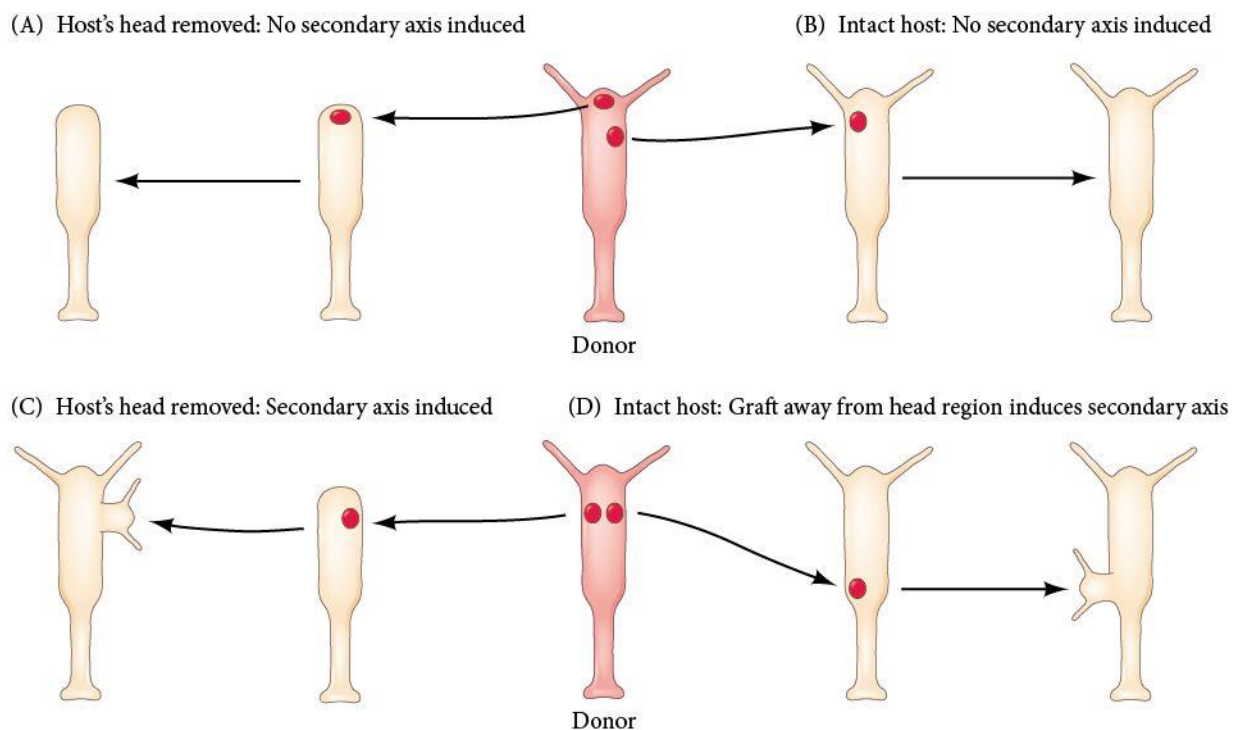


The Head Inhibition Gradients

If any region of the hydra body column is capable of forming a head, how is head formation restricted to a specific location? In 1926, Rand and colleagues showed that normal regeneration of the hypostome is inhibited when an intact hypostome is grafted adjacent to the amputation site (Figure 1A). Moreover, if a graft of subhypostomal tissue (from the region just below the hypostome, where there is a relatively high concentration of head activator) is placed in the same region of a host hydra, no secondary axis forms (Figure 1B). The host head appears to make an inhibitor that prevents the grafted tissue from forming a head and secondary axis. Supporting this hypothesis is the fact that if subhypostomal tissue is grafted onto a decapitated host hydra, a second axis does form (Figure 1C). A gradient of this inhibitor appears to extend from the head down the body column and can be measured by grafting subhypostomal tissue into various regions along the trunks of host hydras. This tissue will not produce a head when implanted into the apical area of an intact host hydra (see Figure 1B), but it will form a head if placed lower on the host (Figure 1D). The head inhibitor remains unknown, but it appears to be labile, with a half-life of only 2–3 hours (Wilby and Webster 1970; MacWilliams 1983a). It is thought that the head inhibitor and the head activator (Wnts) are both made in the hypostome, but that the head inhibition gradient falls off more rapidly than the head activator gradient (see Bode 2011, 2012). The place where the head activator is uninhibited by the head inhibitor becomes the budding zone.



After S. A. Newman. 1974. *J Embryol Exp Morphol* 31: 541-555.

Figure 1 Grafting experiments provide evidence for a head inhibition gradient. (A) Hypostomal tissue grafted to the amputated region inhibits regeneration of the head. (B) Subhypostomal tissue does not generate a new head when placed close to an existing host head. (C) Subhypostomal tissue generates a head if the existing host head is removed. A head also forms at the site where the host's head was amputated. (D) Subhypostomal tissue generates a new head when placed far

away from an existing host head.

But that does not account for the bottom third of the column. What prevents cells there from becoming heads? Head formation at the base appears to be prevented by the production of another substance, a foot activator (MacWilliams et al. 1970; Hicklin and Wolpert 1973; Schmidt and Schaller 1976; Meinhardt 1993; Grens et al. 1999). The inhibition gradients for the head and the foot may be important in determining where and when a bud can form. In young adult hydras, the gradients of head and foot inhibitors appear to block bud formation. However, as the hydra grows, the sources of these labile substances grow farther apart, creating a region of tissue about two-thirds down the trunk where levels of both inhibitors are minimal. This region is where the bud forms (Figure 2A; Shostak 1974; Bode and Bode 1984; Schiliro et al. 1999).

Certain hydra mutants have defects in their ability to form buds, and these defects can be explained by alterations of the inhibition gradients. The L4 mutant strain of *Hydra magnipapillata*, for instance, forms buds very slowly, and does so only after reaching a size about twice as long as wild-type individuals. The amount of head inhibitor in these mutants was found to be much greater than in wild-type individuals (Takano and Sugiyama 1983).

Several small peptides have been found to activate foot formation, and researchers are beginning to sort out the mechanisms by which these proteins arise and function (see Harafuji et al. 2001; Siebert et al. 2005). The specification of cells from the basal region through the body column may be mediated by a gradient of tyrosine kinase, however. The product of the *shinguard* gene is a tyrosine kinase that extends in a gradient from the ectoderm just above the basal disc through the lower region of the trunk. Buds appear to form where this gradient fades (Figure 2B). The *shinguard* gene appears to be activated through the product of the *manacle* gene, a putative transcription factor that is expressed earlier in the basal disc ectoderm (Bridge et al. 2000).

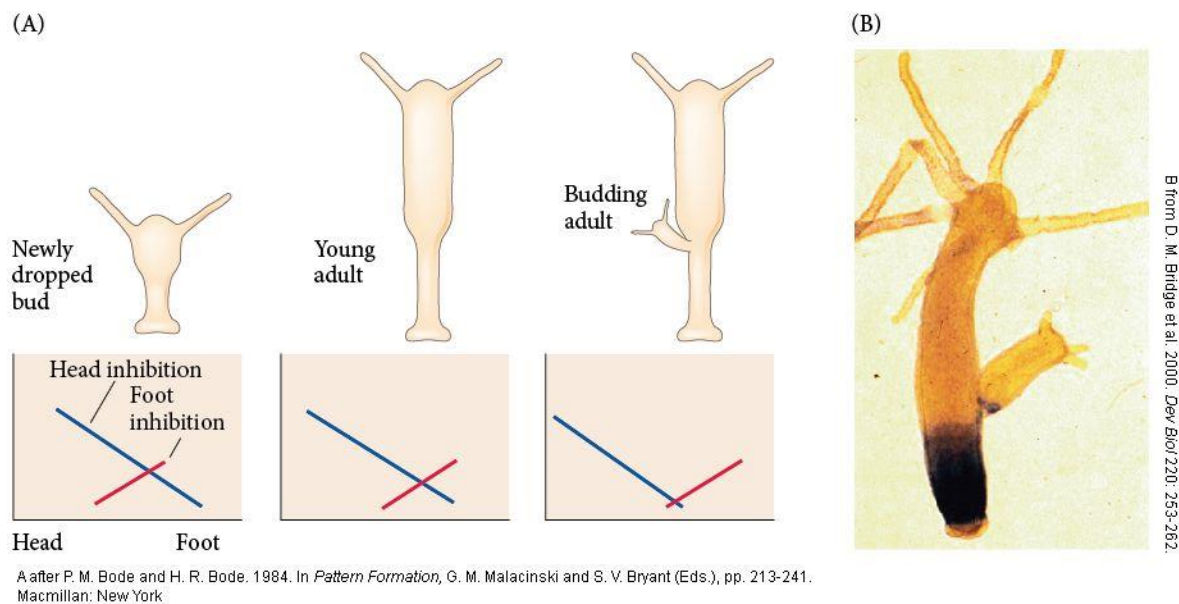


Figure 2 Bud location as a function of head and foot inhibition gradients. (A) Head inhibition (blue) and foot inhibition (red) gradients in newly dropped buds, young adults, and budding adults. (B) Expression of the Shinguard protein in a graded fashion in a budding hydra.

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