Chapter 2
Control of Endocrine Activity

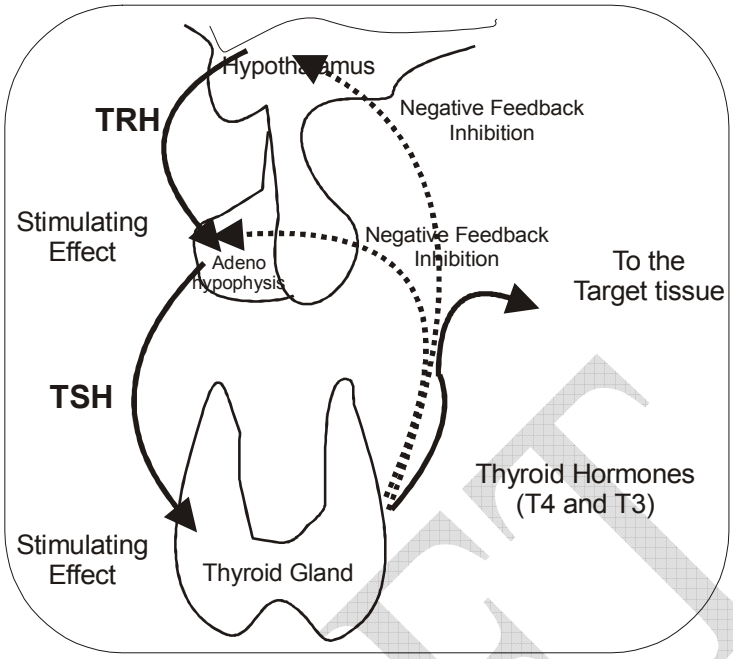
The physiologic effects of hormones depend largely on their concentration in blood and extracellular fluid. Almost inevitably, disease results when hormone concentrations are either too high or too low, and precise control over circulating concentrations of hormones is therefore crucial. The concentration of hormone as seen by target cells is determined by three factors:

- **Rate of production:** Synthesis and secretion of hormones are the most highly regulated aspect of endocrine control. Such control is mediated by positive and negative feedback circuits.
- **Rate of delivery:** An example of this effect is blood flow to a target organ or group of target cells - high blood flow delivers more hormone than low blood flow.
- **Rate of degradation and elimination:** Hormones, like all biomolecules, have characteristic rates of decay, and are metabolized and excreted from the body through several routes. Shutting off secretion of a hormone that has a very short halflife causes circulating hormone concentration to plummet, but if a hormone's biological halflife is long, effective concentrations persist for some time after secretion ceases.

2.1. Feedback Control of Hormone Production

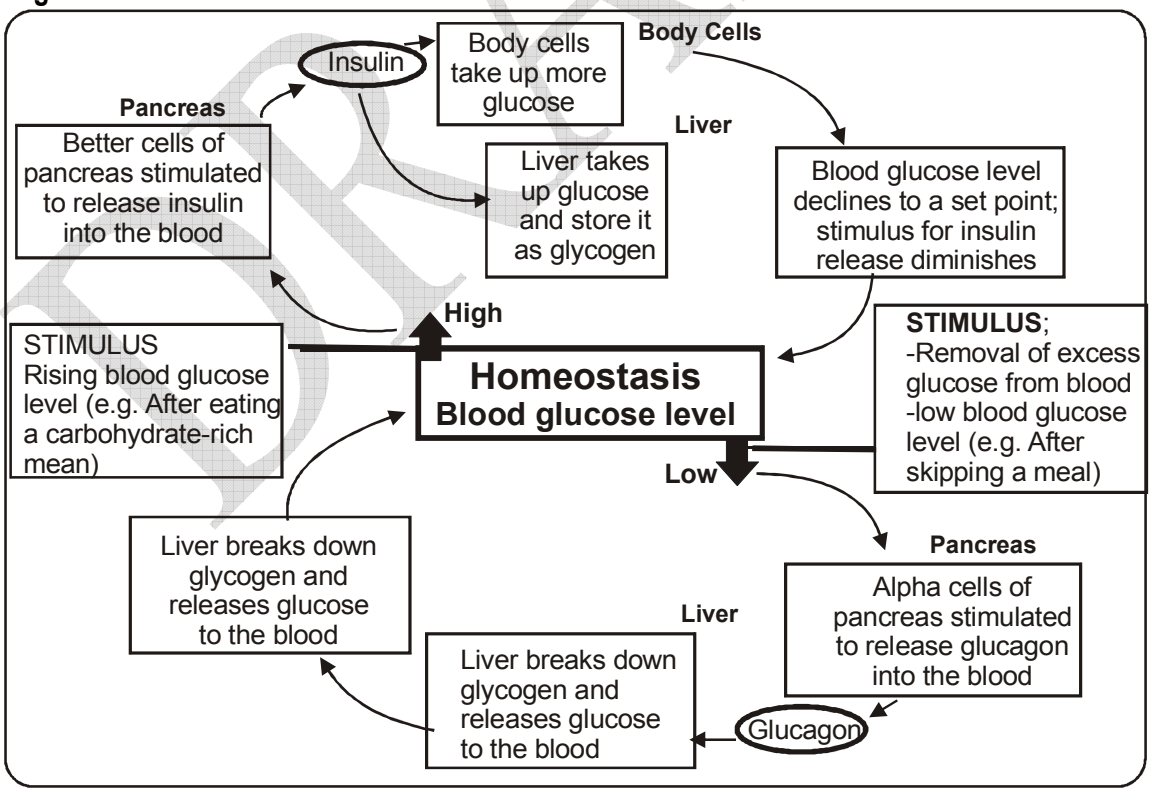
Feedback circuits are at the root of most control mechanisms in physiology, and are particularly prominent in the endocrine system. Instances of positive feedback certainly occur as in LH surge during ovulation, but negative feedback is much more common. Negative feedback is seen when the output of a pathway inhibits inputs to the pathway. Feedback loops are used extensively to regulate secretion of hormones in the hypothalamic-pituitary axis. An important example of a negative feedback loop is seen in control of thyroid hormone secretion. The thyroid hormones thyroxine and triiodothyronine ("T4 and T3") are synthesized and secreted by thyroid glands and affect metabolism throughout the body. The basic mechanisms for control in this system are:

- Neurons in the hypothalamus secrete thyroid releasing hormone (TRH), which stimulates cells in the anterior pituitary to secrete thyroid-stimulating hormone (TSH).
- TSH binds to receptors on epithelial cells in the thyroid gland, stimulating synthesis and secretion of thyroid hormones, which affect probably all cells in the body.
- When blood concentrations of thyroid hormones increase above a certain threshold, TRH-secreting neurons in the hypothalamus are inhibited and stop secreting TRH. *This is an example of negative feedback.*



Inhibition of TRH secretion leads to shut-off of TSH secretion, which leads to shut-off of thyroid hormone secretion. As thyroid hormone levels decay below the threshold, negative feedback is relieved, TRH secretion starts again, leading to TSH secretion .

Another type of feedback is seen in endocrine systems **that regulate concentrations of blood components such as glucose.**



- Glucose from the ingested lactose or sucrose is absorbed in the intestine and the level of glucose in blood rises.
- Elevation of blood glucose concentration stimulates endocrine cells in the pancreas to release insulin.
- Insulin has the major effect of facilitating entry of glucose into many cells of the body - as a result, blood glucose levels fall.
- When the level of blood glucose falls sufficiently, the stimulus for insulin release disappears and insulin is no longer secreted.

Numerous other examples of specific endocrine feedback circuits are presented in the sections on specific hormones or endocrine organs.