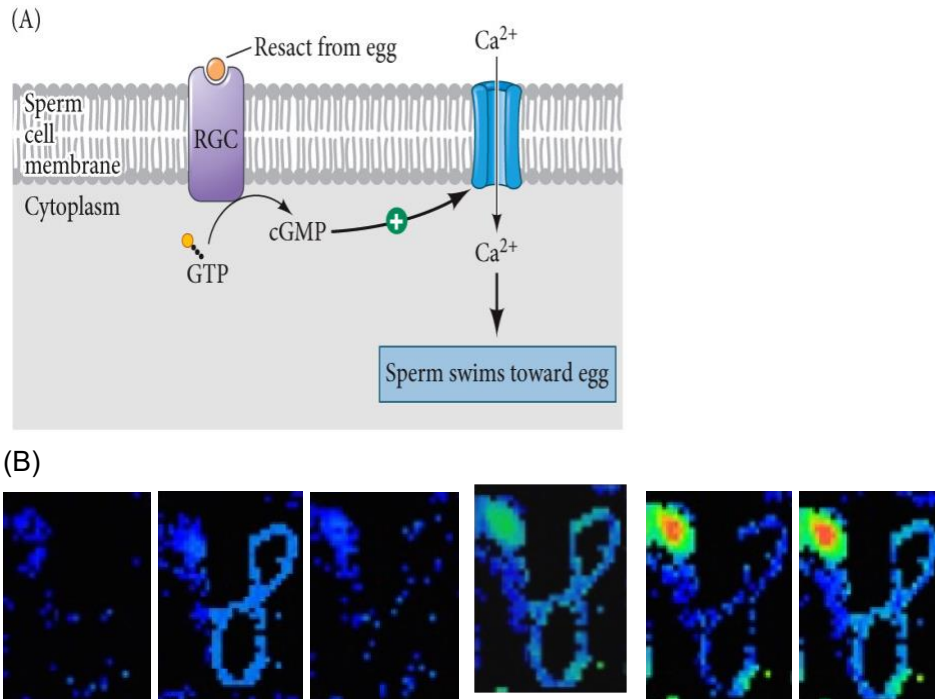


Mechanisms of Echinoderm Sperm Chemotaxis

The mechanisms of chemotaxis differ among species (see Metz 1978; Eisenbach 2004), and chemotactic molecules are different even in closely related species. In sea urchins, sperm motility is acquired only after the sperm are spawned. As long as sperm cells are in the testes, they cannot move, because their internal pH is kept low (about pH 7.2) by the high concentrations of CO₂ in the gonad. However, once sperm are spawned into seawater, their pH is elevated to about 7.6, resulting in the activation of the dynein ATPase. The splitting of ATP provides the energy for the flagella to wave, and the sperm begin swimming vigorously (Christen et al. 1982).

However, the ability to move does not provide the sperm with a direction. In echinoderms, direction is provided by small chemotactic peptides called sperm-activating peptides (SAPs). One such SAP is resact, a 14-amino acid peptide that has been isolated from the egg jelly of the sea urchin *Arbacia punctulata* (Ward et al. 1985). Resact diffuses readily from the egg jelly into seawater and has a profound effect at very low concentrations when added to a suspension of *Arbacia* sperm. When a drop of seawater containing *Arbacia* sperm is placed on a microscope slide, the sperm generally swim in circles about 50 μm in diameter. Within seconds after a small amount of resact is injected, sperm migrate into the region of the injection and congregate there. As resact diffuses from the area of injection, more sperm are recruited into the growing cluster.

Resact is specific for *A. punctulata* and does not attract sperm of other urchin species. (An analogous compound, speract, has been isolated from the purple sea urchin, *Strongylocentrotus purpuratus*.) *A. punctulata* sperm have receptors in their cell membranes that bind resact (Ramarao and Garbers 1985; Bentley et al. 1986). When the extracellular side of the receptor binds resact, it activates latent guanylyl cyclase in the cytoplasmic side of the receptor (Figure 1). Active guanylyl cyclase causes the sperm cell to produce more cyclic GMP (cGMP), a compound that activates a calcium channel in the cell membrane of the sperm tail, allowing the influx of Ca²⁺ from the seawater into the tail (Nishigaki et al. 2000; Wood et al. 2005). These sperm-specific calcium channels are encoded by CatSper genes—the same genes that control the direction of sperm migration in mice and humans (Seifert et al. 2014). The increases in cGMP and Ca²⁺ activate both the mitochondrial ATP-generating apparatus and the dynein ATPase that stimulates flagellar movement in the sperm (Shimomura et al. 1986; Cook and Babcock 1993). In addition, the sperm sense the SAP gradient by curving their tails, interspersing straight swimming with a “turn” to sense the environment (Guerrero et al. 2010). The binding of a single resact molecule may be enough to provide direction for the sperm, which swim up a concentration gradient of this compound until they reach the egg (Kaupp et al. 2003; Kirkman-Brown et al. 2003). Thus, resact functions as a sperm-*attracting* peptide as well as a sperm-activating peptide. (In some organisms, the functions of sperm attraction and sperm activation are performed by different compounds.)



After J. Kirkman-Brown et al. 2003. *Nat Cell Biol* 5: 93–96 (B) from C. D. Wood et al. 2003. *J Cell Biol* 161: 89–101, courtesy of M. Whitaker.

Figure 1 Model for chemotactic peptides in sea urchin sperm. (A) Resact from *Arbacia* egg jelly binds to its receptor on the sperm. This activates the receptor's guanylyl cyclase (RGC) activity, forming intracellular cGMP from GTP in the sperm. The cGMP opens calcium channels in the sperm cell membrane, allowing Ca^{2+} to enter the sperm. The influx of Ca^{2+} activates sperm motility, and the sperm swims up the resact gradient toward the egg. (B) Ca^{2+} levels in different regions of *Strongylocentrotus purpuratus* sperm after exposure to 125 nM speract (the *S. purpuratus* analog of resact). Red indicates the highest level of Ca^{2+} , blue the lowest. The sperm head and tail both show elevated levels of calcium ions within ten seconds.

A chemotactic signaling system should remain unresponsive while the sperm swims through a uniform chemoattractant concentration field and must trigger a directional response only if the cell moves across a concentration gradient. This uniform background is the "noise" encountered by a sperm and should not cause the ubiquitous signals to rise above a threshold needed for activation. In 2020, Ramirez-Gomez and collaborators found that the density of chemoattractant receptors on the sperm cell membrane appears to determine the threshold at which the chemotactic molecule can be sensed. Moreover, the steepness of the chemoattractant gradients provides the coupling force between two physiological oscillators: i) the stimulus function and ii) the internal calcium ion changes. The intracellular Ca^{2+} concentration changes regulate the internal motors that determine the rate of flagellum beating in *Strongylocentrotus purpuratus*, and these are determined by the uptake of the calcium by the receptors. This would also explain species differences in the sensitivity of the sperm to their respective chemotactic agents.

References:

Ramírez-Gómez, H. V. et al . 2020. Sperm chemotaxis is driven by the slope of the chemoattractant concentration field *eLife* 9:e50532.<https://doi.org/10.7554/eLife.50532>

