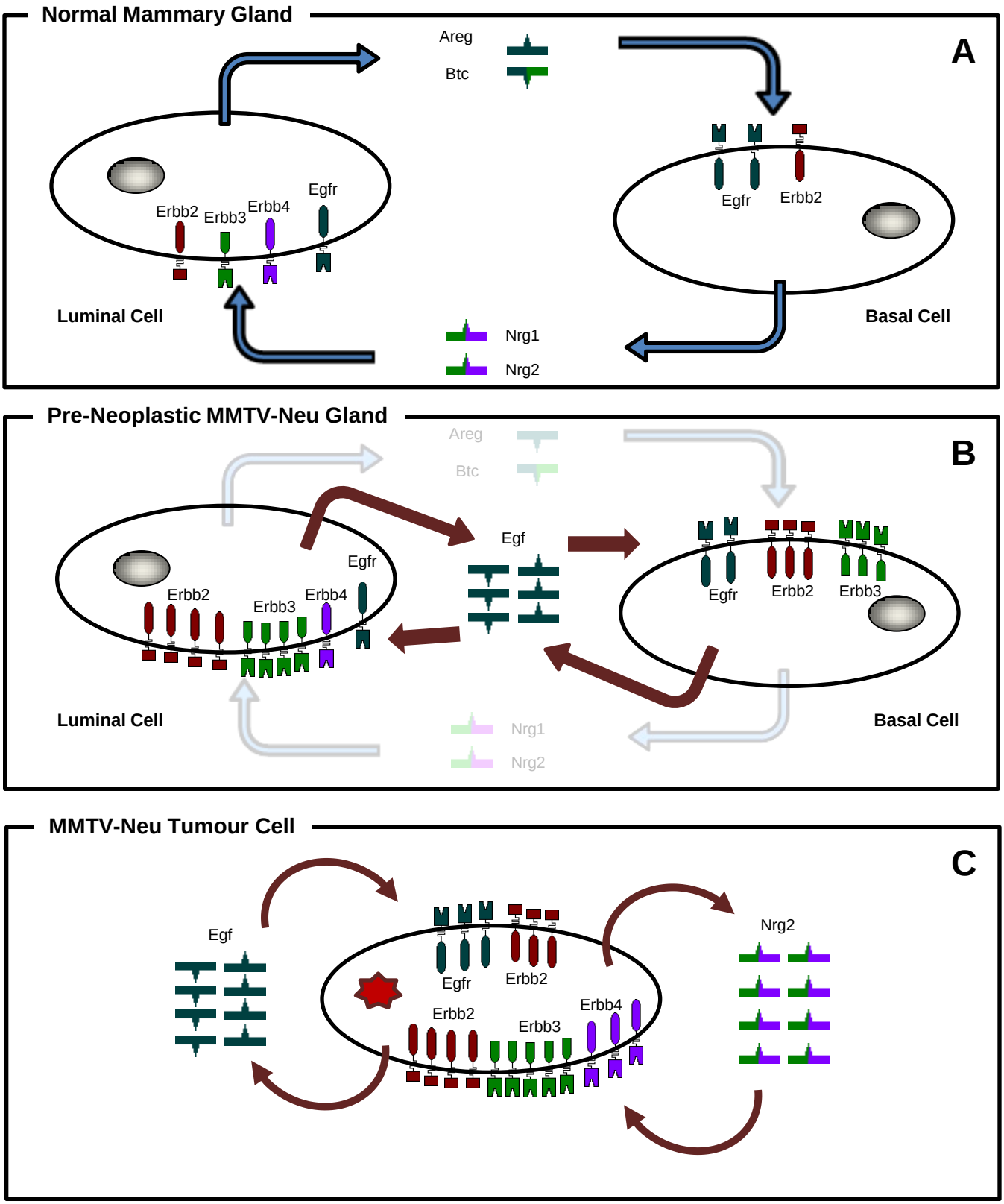

Figure 1. A, Normal mammary gland cell fractions have a paracrine signalling network in which luminal cells secrete ligands (Areg, Btc) recognized by receptors on the basal cells (Egfr); conversely, the basal cells produce ligands (Nrg1/2) recognized by luminal Erbb receptors (Erbb3/Erbb4). Erbb2 has ubiquitous expression and as preferred heterodimerization partner drives cell signalling cascades. B, Pre-neoplastic mammary epithelium in MMTV-Neu mice shows initial anomalies in the signalling network as a consequence of higher production of Egf and Erbb2/3 receptors. C, The switch from paracrine to an autocrine signalling network is completed in MMTV-Neu tumour cells where high levels of secreted Egf and Nrg2 can activate Egfr, Erbb3 and Erbb4 expressed in the same tumour cell. The combination of both high ligand and receptor production (including high levels of Erbb2) results in hyper activation of the Erbb signalling cascade.