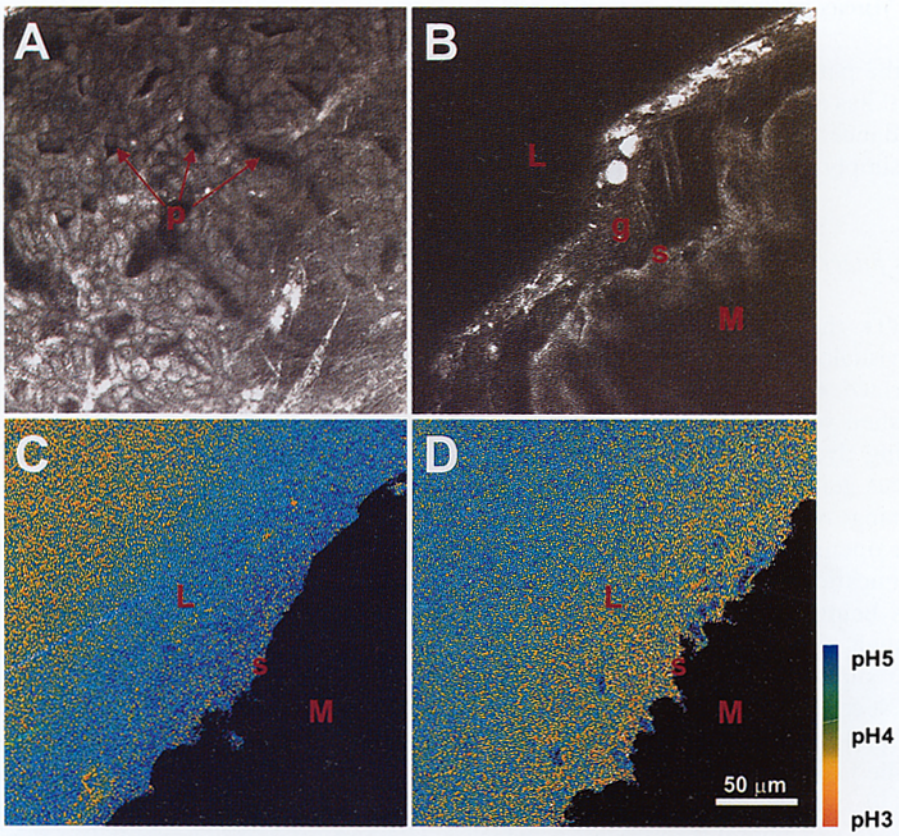

Fig. 1 Imaging gastric mucosal epithelial surface, mucus gel, and surface pH gradient with *in vivo* confocal microscopy. Gastric mucosa of anesthetized rats was superfused with Krebs' buffer containing 0.01 mM NERF (pH-sensitive dye) and 0.5 mM Lucifer Yellow (pH-insensitive reference dye), and excited by a 488 nm laser. (**A**) Confocal reflectance image of the gastric surface epithelium, with openings of single gastric pits (p) and single surface cells detected. (**B**) Confocal reflectance image perpendicular (in the XZ plane) to image (**A**), demonstrating the adherent mucus gel layer (g), apical surface (s) of the epithelial cells, the mucosa (M), and the gastric lumen (L). (**C**) XZ plane emission ratio image of Lucifer Yellow/ Cl NERF (650 nm/ 575 nm) with pH 3 superfusion. The juxtamucosal mucus gel is alkaline. (**D**) The same preparation, superfused with pH 5 solution now shows an acidic juxtamucosal pH.

tures. One of the leading assumptions about the role of gastric mucus is that proton flux across it is asymmetric, allowing the unimpeded outward flow of secreted acid, but impeding inward-diffusing luminal protons. Data supporting the presence of viscous fingers has already been presented, which is one means by which asymmetric transport could be achieved. Other suggested mechanisms include transmucus Na^+/H^+ exchange, in which an opposing flow of sodium ions facilitate acid secretion,[25] and recently, proton trapping by secreted mucus particles, with acid liberated by pepsinogen.[26] All of these theories, however, remain to be tested *in vivo*.

One of the most striking findings, however, is that asymmetric transport mechanisms need not be hypothesized. The inward proton flux (back-diffusion) in the rat when luminal pH = 1, as discussed above, is 0.008 µmol/cm^2/sec.[9] The outward flux of protons during maximal acid secretion is also 0.008 µmol/cm^2/sec in the rat.[27] Similar measurements are also present in dogs.[28] Thus, unidirectional proton fluxes across gastric mucus are equal, suggesting that secreted acid is able to freely diffuse across the mucus layer without the necessity for hypothesizing specialized, asymmetric transport mechanisms. Our *in vivo* confocal data presented above is consistent with simple diffusion of secreted acid across the mucus, since, when superfusion is stopped, a continuous 'acid front' rapidly extends across the mucus layer, with no evidence, in hundreds of observations, of any inhomogeneity.