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Space and time are the prominent attributes of regional science. They show up in all aspects of urban and regional development, including land use policy, environmental management and transportation planning. The present paper aims to offer an integrated picture of the history of regional science in Europe, in the past 25 years. This picture is mapped out in the form of a cascade representation of four interconnected pillars of the edifice of regional science, with a focus on the dynamics in the process of knowledge generation in the field. These four pillars which act as main drivers are: (i) innovation and entrepreneurship (including spatial-economic development), (ii) the geography of movement (including mobility and spatial interaction), (iii) market complexity and spatial flows (in particular, labour and housing markets), and (iv) sustainability in a spatial context (including economic-ecological interactions, resource and climate issues, and social evaluation of plans and projects).