

Evolution of the Immunoglobulin Isotypes – Variations of Biophysical Properties between Animal Classes

Nancy D. Pomarici¹, Roberta Cacciato¹, Janik Kokot¹, Monica L. Fernández-Quintero^{1,*} and Klaus R. Liedl¹,

¹Institute of General, Inorganic and Theoretical Chemistry, Center for Molecular Biosciences Innsbruck (CMBI), University of Innsbruck, Innrain 80-82, A-6020 Innsbruck, Austria.

*Correspondence: Monica.Fernandez-Quintero@uibk.ac.at, Klaus.Liedl@uibk.ac.at

Ch1 domains accession codes:

CAC43066; NWZ28413; KFQ46330; NWI29386; KAI6061223; NXD18504; QAT77293; AAA68606; NXA57377; AEF79983; AMS75109; ASU87373; APB61243; AFZ39218; AAB22614; AFZ39174; AFZ39211; AFA41928; AFZ39189; AFZ39165; AFZ39193; AFZ39176; AFA41929; KAF7235451; ABG72683; CAC20453; P01876; PNI15543; AAB30803; AAB59396; CAA37745; CAA37741; CAA37744; P20758; CAA37743; CAA37746; AAQ62620; ABI97137; ABI97140; ABI97138; ABI97139; QJB76121; QJB76122; CAA37742; ABK15554; ABI97146; ABI97149; AAK72414; ABI97145; AAK72413; AAK72412; AAQ62621; AAT11507; AAK72410; ABI97144; ATV90895; ABI97143; ABI97142; ABI97141; AAK72411; QJB76118; AAC64980; AAT65195; AAC98391; ADD51207; AAA65943; AMP34155; ELR44852; NIG60332; ATI97333; ATI97345; ATI97346; ATI97338; ATI97337; AAA56796; KAI5162510; AAX73304; QJY40729; CAO79580; ADD71719; ELK01275; KAF6072915; AAP80145; P0DUB3; EPQ16373; AQR55605; AQR55606; BAL70397; AQR55608; AQR55609; ALB75436; ELK36012; EHB17602; ELV12711; QGV56640; EHB08048; KFO35296; AGN11433; KAG8525088; AAL15540; AAL15539; AAD41690; AAB84185; AAL17701; AAN33012; AAL17700; AAC48835; AAD21190; BAD34542; BAD34541; ACO88906; AFQ38975; AFI33218; AXL14358; UZS59180; AHY86392; AFZ39186; AFZ39208; APB61242; AKM28416; AFR33844; ABY67439; BAV35204; BAV35207; ABC75541; AIW06017; AAB21246; PNI88328; PNJ04970; ABB89457; ABB89464; ABB89458; ABB89461; ATV90901; XP_032123471; ABB89467; AAN07167; AAN03672; QJY40730; AAU09793; XP_043413080; AAX73311; AAN07165; XP_044789334; AMP34156; AAN03671; ANN46372; AAN03673; AAB59653; AAO19643; AES92971; AES92974; AES92977; AES92976; AES92973; AES92972; AGY29606; AGG53192; AGY29601; AGY29615; AGY29616; AGY29605; AGG53194; AGG53198; AGG53201; AGG53184; AGG53222; AGG53231; AGG53219; AGG53227; AGG53223; AGG53202; AGG53218; AGG53226; AGG53229; AGG53224; AGG53195; AGG53185; AGY29603; AAB03680; BAJ20182; BAJ20183; AGG53193; AGG53204; AGG53186; AGG53199; AGG53206; AGY29600; AES92963; AES92968; AES92981; AGG53211; AGG53212; AGG53207; AGG53208; AGG53213; AGG53217; AES92962; AES92979; AGG53203; AES92982; AAT02197; AES92983; AES92970; AES92967; ACU45375; AFR90288; AFR90269; AFR90270; AFR90264; AFR90268; AFR90274; AFR90279; AFR90257; AFR90258; AAB59395; P01854; P0DOX4; AEG78107; AAA35416; ATV90896; AEG78114; AEG78120; AEG78096; AEG78100; AEG78105; AEG78110; AEG78095; EGW12809; AEG78093; AEG78099; CAC44499; AEG78094; AAA85662; AAF43901; AAA53301; AEG78097; QGU21335; QGU21326; QGU21344; QGU21334; QGU21345; QGU21347; QGU21352; AEG78098; QGU21351; QGU21350; QGU21342; QGU21318; QGU21322; QGU21317; QGU21325; QGU21333; AEH26435; KAF0884900; AAA41364; P01855; QGU21320; QGU21321; AAX73306; QGU21280; QGU21289; QGU21348; QGU21309; CAO79579; AAA56797; QGU21307; QGU21302; QGU21287; QGU21349; ELK01276; AEG78103; AEG78101; KAG8525035; ELK37506; ALB75437; KAH0514093; QGV56638; KAF6500411; CAA81788; KAI5936975; ELV12710; P06336; BAQ55489; KAI5162512; QJY40731; KAF6273895; KAF6279810; BAM66311; KAF6268940; AAO37095; AAB09546; AAL17702; ELR44851; AAA51378; AAM45140; AAC79674; EPQ01894; PNI15546; AXN93645; AXN93652; AAG00910; PNJ01622; 5DK3; AXN93654; PNJ04973; AAF14058; PNI15539; AAT11504; AAM93486; AAT11502; AAM93487; PNI15541; CAC20457; AIL50394; AAT11503; AAM93488; AAM93489; AAQ57562; AGC00826; AAT11505; AAF14060; AAG00912; AIK19747; AGC00825; AGC00822; ATV90899; ACO54886; AGC00821; AAQ57556; CAC20456; QNM80716; AGC00823; QJB76128; ATV90897; AGC00827; AIM44673; AIM44672; MBZ3888618; AAL35302; EHB08049; AAS18414; AIM44676; AKM12424; AAB59265; AKM12428; AIM44631; ABD64612; AYM94157; AAL35303; ADD71697; BAA32230; CAC44763; XP_042845222; AIM44657; AIM44666; AIM44652; BAI82568; BAM75541; BAM75540; AIM44639; AAX73307; AAA52216; BAM75546; BAM75565; ABY85807; ATI97579; AHH34165; AHA35861; AIM44674; AIM44675; AIM44644; AIM44661; AIM44662; AAA52219; P01862; AAG42243; BAM66310; ALB75439; ADX94416; AAA30965; ABY85805; ATI97593; AQR55684; ACD64981; AAX73308; AAA51294; P20759; P20760; ABD64610; ADX94417; KAB1277999; AIM44671; EHB08050; ALB75438; KFO35298; NIG61489; EPQ16374; CAC44760; CAC44624; AAP82181; AAL35301; AAL35304; EGW12805; BAM66309;

AAA51295; AAA82733; AAG01011; AAB37381; EPQ01893; CAO79572; ABE68619; AQT27060;
 EPY72686; AQT27058; CAC86339; CAC86340; KAH0514073; ANN46376; P20762; ADZ32495;
 ACO52352; AAB59697; BAA03476; AAT65197; AAC48761; CAA49451; BAM66305; EGW12808;
 AAC48762; AAB59660; ANN46375; AAT65196; ABY85808; AAB37380; ANN46379; AQT27056;
 BAI82569; AWY10546; ABD73925; AAA37906; AAA60738; AQT27057; CAC86341; EGW12806;
 CAA34864; QGV56636; AAB59658; ABQ85912; CAA47649; KAG8519298; AAB59656; P01868;
 BAL70394; ADX94418; KAI5162393; AAL17703; AAL17704; AAD55590; ACX54357; AAM61760;
 QWC92995; AFR90251; AFR90252; AFR90253; AFR90246; ACU45374; AFR90247; AFR90248;
 AFR90245; AFR33767; AFR33765; ABV66132; AFR33766; ABV66129; AIW06024; AIW06020;
 AIW06021; AIW06022; CAE02686; BAV35203; CAA49247; AFZ39171; AFZ39181; AFA41930;
 AFZ39220; AFZ39182; KAI6061222; CAA46322; APB61246; APB61247; AMS75110; AHZ12733;
 AKM28417; QAT77294; AFZ39169; AFZ39170; AFZ39180; AFZ39224; KYO29711; BDI00299;
 ABW77756; ABY54906; AAC59687; XP_039855852; ABD76396; AEH76773; ABW89619; ABW81216;
 ACA51888; XP_037834750; ACM90147; AAL99929; ABW81218; XP_026021082; ABW89622;
 ANO53445; XP_037544448; ABW81220; AAL99934; AHC31440; XP_025762367; XP_025762368;
 AHY86391; XP_042565114; AAC59688; MBN3322266; RXN05506; AHI18415; TSK87411; QHO62363;
 BAB60868; BCU66532; ARC77253; QDP16243; APJ36370; KAF5906456; AOW44096; AOW44093;
 AOW44094; UUY86300; KAA0705619; XP_029913635; XP_029913634; XP_029913633; AFA41926;
 QAT77292; AMK48542; APB61245; AMS75108; NXW26075; APB61244; NWS64666; CAC43281;
 ASU87372; ASU87371; KAI6061224; AFZ39177; AFZ39178; AFZ39179; AFZ39216; ABV66128;
 ABY74509; AFR33764; AFR33841; KAG8140957; XP_017945116; BAV32322; CAE02685; AAA49878;
 AIW06014; AFM37312; CAC20458; PNJ04967; PNI10622; QJB76129; AAD02420; KAH0514101;
 EGW12804; AAB59651; CAA27326; QGU21427; QGU21428; QGU21429; QGU21431; QGU21430;
 QGU21377; QGU21356; QGU21366; QGU21374; QGU21364; QGU21382; QGU21358; QGU21397;
 QGU21360; QGU21353; QGU21355; QGU21359; QGU21375; AAU09792; QGU21407; QGU21398;
 QGU21426; QGU21420; QGU21413; QGU21404; QGU21405; QGU21403; QGU21402; QGU21432;
 KAI5934885; KAI5936976; KAI5162392; BAL70395; P06337; AAG40853; EPQ16375; MBZ3882660;
 KAI5936977; BAA32231; ANN46370; AAB09545; AAX73309; QJY40733; KAG8519297; AAA51379;
 CAO79569; AAO37096; EHB10927; AAB62251; ADD71716; ABX89978; ALB75443; CAA42611;
 EHB11820; QGV56635; KFO35302; BAD00196; AIA77883; AAF80358; BAM66301; AAC48775;
 QWC92960; QWC92964; AAD21191; AAO37747; AAD24482; P20768; AAN33013; XP_041031595;
 AGG53273; ABW84256; AES92946; ABW84248; AGG53275; AGG53277; AGG53281; ABW84251;
 AAU04508; ABW84249; AGG53282; AGG53286; AGG53285; ABW84252; AGG53279; ABW84254;
 AES92940; AGG53276; AGG53278; AES92935; AES92956; UTD43067; AES92941; AES92937;
 ABW84253; BAJ20181; AES92934; AES92945; AES92955; AES92957; AES92939; AES92951; AES92944;
 AES92947; AES92936; AES92950; AES92954; AES92943; AEJ86609; AEJ86613; ABW84255; AAK07642;
 ABW84250; AES92952; AAB04673; AEJ86611; AEJ86616; AEJ86614; AEJ86607; AEJ86608; AEJ86600;
 ACU11614; AEJ86610; ACU11613; ACU11612; AEJ86605; AEJ86601; AEJ86599; AEJ86615; AEJ86629;
 AEJ86606; ACU11611; AFR90255; EMP41995; AAB03838; ACU45376; 2RCJ; AAB48195; ABB83616;
 AYN64868; AYN64869; AES92988; AES92986; AES92959; AES92984; AES92989; AES92987; UTD43068;
 BAJ20187; AGG53233; AGG53246; AGG53238; AGG53232; AGG53260; AGG53264; AGG53263;
 AGG53261; AAT02204.

Ch3 domains accession codes:

NWZ28413; KFQ46330; CAC43065; NWI29386; KAI6061223; NXD18504; QAT77293; NXA57377;
 AEF79983; AMS75109; ASU87373; OWK49842; APB61243; AFZ39218; AAB22614; AFZ39174;
 AFA41928; CAC43064; AFZ39189; EOA93117; AFZ39165; AFZ39193; ACE79178; AFZ39176;
 AFZ39219; AFZ39210; AFZ39190; AFA41929; 6UE7; CAA37745; CAA37741; CAA37744; CAA37746;
 6UE8; AAQ62620; QJB76121; ABI97146; QJB76120; ABI97143; AAK72411; ATV91193; AAC64980;
 AAT65195; AAC98391; BAD67216; MBW04533; AMP34155; ELR44852; NIG60332; ATI97333;

AAA56796; KAI5162510; ATI97347; KAF0884899; KAI5936974; KAB1277053; AAX73304; QJY40729; CAO79580; ADD71719; ELK01275; KAF6072915; AAP80145; P0DUB3; EPQ16373; AQR55605; BAL70397; AQR55608; AQR55607; ALB75436; ELK36012; ELV12711; EHB08048; KFO35296; AGN11433; AAA41375; AXM43016; ELK37507; P01879; AXM43009; AAL15542; AAL15540; AXM43013; AXM43008; AXM43012; AXM43015; AXM43014; ABV01995; AAD41690; AAB84185; AAL17701; AAN33012; AAL17700; AAC48835; AAD21190; QWC92952; QWC92951; BAD34542; ACO88906; AFQ38975; AFI33218; AXL14358; UZS59180; AAL79934; AHY86392; KAG7506059; AFR33844; ABY67439; AIW06017; AIW06018; AAB21246; P01880; PNI88328; PNJ04970; ABB89457; ABB89461; ATV90901; XP_032123471; ABB89467; AAN07167; QJY40730; AAU09793; XP_043413080; AAX73311; KFO35301; AAN07165; XP_044789334; AMP34156; AAN03670; AAN03671; AAB59653; AAO19643; AES92971; AES92974; AES92977; AES92975; AES92976; AES92973; AES92972; AGY29606; AES92978; AGY29601; AGY29615; AGY29605; AGG53222; AGG53223; AGG53228; AGG53230; AGY29603; AAB03680; BAJ20182; BAJ20184; ACU45375; AFR90280; AFR90266; AFR90268; AFR90291; AFR90290; 4GRG; 5NQW; 5LGK; P0DOX4; AEG78107; AEG78109; AAA35416; ATV90896; AEG78114; ATV91162; AEG78112; AEG78120; AEG78096; AEG78105; AEG78110; AEG78095; AEG78116; AEG78117; AEG78118; AEG78093; AEG78099; BAL70396; CAC44499; AEG78094; AAA85662; AAF43901; AAA53301; AEG78097; QGU21335; QGU21345; QGU21347; QGU21352; AEG78098; QGU21351; QGU21350; QGU21342; QGU21322; QGU21324; AEG78104; QGU21346; KAF0884900; BAB40315; QGU21320; AAX73306; QGU21280; CAO79579; AAA56797; QGU21279; QGU21307; QGU21349; QGU21291; ELK01276; CAO79578; AEG78103; KAG8525035; KAB1277055; ELK37506; KAH0514093; QGV56638; KAF6500411; CAA81788; AAA37916; AAA37912; KAI5936975; ELV12710; AAZ05128; BAQ55489; KAI5162512; QJY40731; KAF6273895; KAF6279810; BAM66311; EHB16230; KAF6268940; KFO35297; AAO37095; AAD27886; ANN46381; AAL17702; ELR44851; AAA51378; AAM45140; AAC79674; AAC78140; ABV01996; 1SY6; 5HSF; AAD38158; PNI15546; AXN93645; AAB86467; PNI15544; CAA43606; QNT08899; 7RHO; 5U4Y; 4BM7; 4DZ8; 7Q15; 4DZ8; AAG00910; AAB21082; PNJ01622; 7LUS; 5DK3; AXN93654; PNJ04973; AXN93657; AAF14058; PNJ04971; PNI15539; 7LUS; AAT11504; AAM93486; 4B53; PNI15541; CAC20457; BCY27132; AAA18103; AIL50394; AGC00824; AAT11503; AAM93488; AAM93489; AAQ57562; AGC00826; 6D58; 5W38; 6D4I; AXN93656; AAF14060; AAG00912; AIK19748; AIK19749; AIL50396; AIL50395; AIL50393; AGC00825; AAQ57565; AGC00822; QEV83695; CAA67886; QJB76126; AIK19746; AIL50397; AGC00821; AAQ57556; QJB76127; CAC20456; AAF14059; 5HVV; QNM80716; 6WMH; AGC00823; QJB76128; AAQ57570; AGC00827; 6WOL; 5K65; MBZ3888618; AAS18414; AIM44676; AAA31288; XP_051697838; AKM12436; AAA64252; BAA32230; CAC44763; CAC44762; XP_042845222; AIM44657; AIM44668; AIM44652; AIM44637; AIM44670; BAI82568; CAO79576; CAO79577; AIM44650; AIM44669; AIM44639; AIM44641; AIM44638; AIM44651; AIM44659; AAX73307; ABY85810; AAA52216; BAM75546; BAM75560; ABY85807; ATI97578; ATI97579; AHA35861; AIM44674; AIM44675; AIM44658; AIM44644; AIM44660; AIM44661; AIM44662; ABW89018; AAA52219; P01862; AAG42243; BAM66310; ALB75439; ABY85806; ADX94416; AAA30965; AAA51281; ABY85805; ATI97593; KAF0871663; AQR55684; AAX73260; CAO79571; BAE20056; AAA52220; AAX73308; AAA51294; CAO79570; AAA41373; AAA41376; BAM75571; ATI97556; KAB1277999; AIM44671; KAB1277054; AAX73259; EHB08050; ALB75442; ADX94415; KFO35298; NIG61489; EPQ16374; CCF72130; ALB75440; CAC44760; ALB75441; AAP82181; AAL35301; AAL35304; EGW12805; AAY98508; BAM66309; AAA82733; AAG01011; ELK30486; AAB37381; EPQ01893; CAO79572; ABE68619; EPY72686; CAC86339; CAC86340; KAH0514073; ANN46376; CAO79573; ADK11691; ADI87159; KFO35299; QJY40732; P20762; ACO52352; ADZ32494; AAT65197; ELK24149; AAC48761; CAA49451; BAM66305; EGW12808; AAC48762; AAB59660; ANN46375; P01865; KAB1278001; ACS34824; ANN46374; AAT65196; ABY85808; AAB37380; ANN46379; AQT27056; BAI82569; ANN46378; ACO52350; ABD73925; AAA41374; AAA37906; AAA37907; AQT27057; CAC86341; CAA24176; AAD40243; EGW12806; CAA34864; QGV56636; ACO52351; ACO52349; AAH92269; KAG8519298; KAB1252581; P01867; CAA39804; AAB59657; BAX57196; QGV56637; BAL70394; AAC36504; ADX94418; KAI5162393; KAI5162394; ELR44850; KAI5162514; AAL17703; AAL17704; AAD55590;

ABV01997; ACX54357; AAM61760; QWC92995; AFR90251; EMP30595; AFR90250; AFR90246; ACU45374; EMP30114; AFR90247; EMP40110; ALU11324; AFR33767; AFR33765; ABV66132; AFR33766; ABV66131; AIW06027; AIW06026; AIW06024; AIW06023; CAE02686; BAV35203; CAA49247; AFZ39171; AFZ39181; AFZ39200; AFZ39223; AFA41930; AFZ39220; KAI6061222; AFZ39221; CAA55148; APB61246; APB61247; NXK71518; AMS75110; AHZ12733; AKM28417; QAT77294; AFZ39169; AFZ39170; NXP02446; AFZ39180; AFZ39224; KYO29711; BDI00299; AEJ86627; ABW77756; ABY54906; AAC59687; XP_039855852; ABD76396; AEH76772; AEH76773; ABW89619; AEJ86624; ABI18250; ACA51888; AEH76774; XP_037834750; ACM90147; AAL99929; ABW77754; XP_026021082; ABW89622; ANO53445; XP_037544448; ABW81220; AHC31440; XP_025762367; XP_025762369; AHY86391; XP_042565114; AAW71781; AAC59688; MBN3322266; RXN05506; TSK87411; QHO62363; BAB60868; BCU66532; ARC77253; QDP16243; APJ36370; KAF5906456; AOW44096; AOW44093; AOW44094; UUY86300; KAA0705619; ATG71407; XP_029913635; AFA41926; AFA41927; QAT77292; CAC43068; CAC43062; EOA92985; AMK48542; APB61245; AMS75108; NXW26075; APB61244; NWS64666; CAC43281; ASU87372; AAA68605; ASU87371; KAI6061224; KQK84655; CAC43061; AMS75107; AFZ39177; AFZ39206; AFZ39178; AFZ39212; AFZ39179; AFZ39217; AFZ39213; ABV66128; KAF7235453; ABY74509; KAG8140955; AFR33764; AFR33841; KAG8140958; KAG8140957; XP_017945116; BAV32322; CAE02685; CAL92494; BAV32323; AAA49878; AIW06014; AIW06015; 7QDO; 7K0C; PNJ04967; PNJ04968; PNI10622; QJB76129; ATV91186; AAB59421; ATV91189; AAB59422; KAH0514101; EGW12804; CAA48392; 8E4C; 4JVV; CAC20701; AAA37908; AAA31293; MBW04751; QGU21427; QGU21428; QGU21429; P04221; QGU21367; AAU09792; QGU21407; QGU21432; QGU21363; QGU21416; QGU21406; ABQ42870; KAI5934885; BAL70395; P06337; AAG40853; EPQ16375; MBZ3882660; KAF6273897; EPQ01892; KAI5936977; KAF6273896; BAA32231; ANN46370; AAX73309; QJY40733; ANN46368; BAD00197; KAF6072922; KAG8519297; AAA51379; BAD00199; CAO79569; AAO37096; EHB10927; AAB62251; ANN46369; KAF6072921; ADD71716; ABX89978; BAD00198; CAA42611; EHB11820; KFO35300; QGV56635; KFO35302; QGV56641; BAD00196; AIA77883; ACS29496; ABV01998; AAF80358; BAE20181; AAA51297; QWC92960; AAD21191; AAO37747; AAD24482; AAC48834; CAA32113; AAN33013; ELK18451; XP_041031595; AGG53273; AGG53270; ABW84256; AGG53267; AES92946; ABW84248; AGG53275; ABW84251; ABW84249; AGG53286; AGG53279; AES92940; AGG53276; AGG53278; AGG53283; AES92935; AES92956; UTD43067; AES92941; AES92937; ABW84253; BAJ20181; AES92934; AES92945; AES92955; AES92957; AES92942; AES92944; AES92947; AES92950; AES92954; AES92943; AEJ86609; AEJ86613; ABW84255; AAK07642; ABW84250; AES92949; BAJ20180; AES92952; AES92933; AES92953; AEJ86612; AAB04673; AAB04672; AEJ86611; AEJ86616; AEJ86614; AEJ86607; AEJ86608; AEJ86600; ACU11614; AEJ86610; ACU11613; AEJ86603; AEJ86601; AEJ86599; AEJ86615; AEJ86604; AEJ86629; AEJ86606; AEJ86602; ACU11611; AFR90255; EMP38542; AAB03838; AFR90254; ACU45376; 2RCJ; 4Q9C; AYN64868; AYN64869; AES92988; AES92986; AES92959; AES92958; AES92984; AES92989; AES92987; UTD43068; BAJ20187; BAJ20186; AGG53233; AGG53242; AGG53246; AGG53244; AGG53234; AGG53260; ACZ65035; AGG53241; AGG53264; AGG53261; AGG53254; AAT02204.

Cl domains accession codes:

ACN09846; AWO67269; XP_047018211; XP_051739581; RXM94251; AWO67273; AWO67285; KAG8013225; KAG8013225; ACO13580; XP_050934017; ROI42561; ROL42386; ROL45405; ROL45405; ROL45405; TKS88155; KAG8003810; RXM36454; ACM09554; TKS80340; KAG8004842; ACO14165; ROI42554; KAG1948728; TKS80331; KAG8005388; KAG8005388; TWW70092; TWW52955; TWW52950; TWW70105; TKS80337; ROL45834; KAG1948731; ROL45835; TKS80333; TKS65975; ROL45837; KAG8000903; KAG8004815; KAI2646515; KAI2652986; KAG8015005; KAG8004848; KAG8004813; KAG8004844; KAF3707015; KAG1929366; KAG1929376; XP_017209378; KAF3707045; KAF3706995; KAF3706993; XP_049331886; XP_019209278; KAG8014350; KAI2652987; KAI2652987; 7PI2; AMN08822; XP_033024710; XP_028558593; XP_028607806; XP_031760076; XP_044151386;

XP_044151388; XP_029436932; 6XJA; PNI16580; AAD29610; AAB32987; AAD15786; BAC01684; BAC01702; AKL91152; QBK47591; BAC01749; BAC01680; BAC01723; BAC01672; BAC01713; BAC01707; BAC01737; BAC01692; BAC01709; BAC01732; BAC01676; AAA70229; BAC01752; BAC01698; BAC01694; BAC01724; BAC01699; BAC01722; BAC01714; BAC01704; BAC01695; QBK47577; BAC01690; AAC17968; AAB50880; 5VSI; XP_030864111; BAK48744; 6WGG; QJB76131; AFF60184; ATV91331; ATV91107; ATV91333; CAH17921; AAA18107; ACN96923; ACN96925; ACN96964; ACN96922; ACN96929; ACN96954; ACN96955; ACN96965; ACN96921; ACN96931; ACN96920; ACN96927; AAO84649; CAA53284; KAI5140899; AAA03520; P01835; AAO84653; ELK10654; ABV48920; AAA41405; KAG8512959; QJY40727; AAA41404; AAA41402; AAA39011; ABD64609; AAA39008; AAC37305; AAA41406; AAA41408; AAA39012; AAA39007; 6PYC; AAL17618; 6YHQ; KAI5939771; P01837; AAA38809; AWY11552; ABW24728; AAX47168; BAB90992; AAB53777; 1FPT; CZF87190; 3J42; XP_026908457; AAU45094; 7TOL; AAG43418; AAA41407; ABW24722; AAD40242; CAA24192; AAY83834; AAG43420; AAB53778; CAN87019; AAK01030; AAC98953; 1QFU; EHA99433; ABV02006; ABV02004; ATI97435; ATI97443; CAA38046; 3I50; AAF04610; AAA41403; AEM45012; AEM45004; ELR47093; ATI97444; EGW03655; KFO32621; AAA82732; KAH0519255; MBZ3873919; AAA31358; AAA31335; CCF72150; ELV10784; AAA51333; CAA88305; 6P62; KAB1256817; AAA31334; CAA10920; AAA31357; P01840; AAA31350; AAA31336; P03984; P01838; ABD64611; P01841; AAA31333; 7R8U; XP_048449493; XP_041035061; EMP26807; TFJ95003; XP_039353321; XP_049323828; KAI2648002; KAI2647426; KAI2647787; ROI42558; RXM98356; ROJ13904; KAI2648147; ROI42566; KAG8013240; XP_017315847; TMS15304; AWO67301; KAE8283257; TKS92024; XP_045066922; XP_021330477; TKS92025; ROL53049; TKS92023; KAE8283263; ACI66966; XP_021176414; XP_035035602; KAE8290125; ROL53045; XP_036797802; XP_045074771; KAG7504299; XP_014264359; KAF3700111; KAF3688195; XP_047199938; KAG8010901; KAG8010900; XP_034150846; XP_024658106; TSO37091; KAI2666591; KAI2646143; RXM95833; XP_047197646; XP_036006869; XP_036811263; KAF5883633; ROL44084; XP_024658107; KAG8010896; KAE8283260; TWW54037; TWW71864; KAF3706994; TWW54253; TWW53820; KAG8013218; TWW71862; KAG8013228; KAG8013229; KAG8013215; KAG8013236; KAG8013223; XP_024661989; XP_025759058; TWW53084; KAA0701453; XP_025756606; KAA0710206; XP_019212893; KAA0710207; KAA0710207; KAG1972221; AFA41931; XP_027669870; XP_050570205; KFQ94409; AMN08825; KFO05719; KFQ33173; KFU89639; KAF1663710; QAT77297; ARX27859; KFW96158; AMN08826; AMN08824; KFO13525; AMN08823; KFW81604; KFQ94410; P20763; AAA48906; XP_021405632; ACH44209; ACH44210; XP_035746355; XP_050565204; XP_015677573; XP_015677573; KAG8146258; KAG8146258; KAG8146257; KAG8146257; KAG8146257; KAG8146259; KAG8146259; ETE68561; AAK07180; XP_033812901; XP_030043573; XP_033812642; XP_040261465; XP_030047891; XP_030045028; XP_033779923; XP_040180289; XP_029441631; AAO20093; AAO53356; P01843; AAO53357; AAO53417; AAO53418; AAO53416; AAA40096; AAO53347; P20766; AAA41419; XP_015442277; KAB1255245; CCN25613; AAO53393; AAR88376; KAI5929959; AAB24270; ELK15590; CAA40948; ABV22589; BAC01828; AAA59109; 4LLD; AAA58999; ABU90693; ABU90732; ABU90589; BAC01825; BAC01851; BAC01852; BAC01774; QJY40728; QJB76132; P0CF74; ATV91490; KAF6403527; XP_012997011; AAA30966; XP_023618956; QNT08900; ACN96934; 4LLM; ACN96935; 4LLQ; ACN96974; P01847; ACN96968; BAC01773; ACN96967; BAC01861; ABU90579; ASL06610; ABU90680; ACN96969; QBK47527; ABU90623; ANN81988; AEO16798; BAC01780; 4LLY; BAC01816; BAC01802; QCR98082; BAC01776; BAC01824; BAC01775; BAC01821; BAC01769; BAC01860; BAC01862; BAC01817; BAC01813; QCR98083; BAC01779; AAB28401; XP_012417851; ATV91493; ATV91491; KFO34801; XP_045220380; ACN96937; ACN96975; ACN96977; ACN96941; ACN96936; BAC01770; BAC01850; MBV95923; CAA27229; KAG8514505; CAA92268; AAB36578; ELK26785; EPQ11107; P01846; ELW49661; XP_044897840; ELK26787; ELK26786; AAA31360; AEM05840; AAA50983; XP_006768346; AAA31362; AAA31361; EGW07544; AIY24756; AEM05845; AEM05849; AAU45093; AIY23700; AEM05841; AET14246; AEM05838; AAK84156; AAA50971; AET14244; AET14243; AET14245; CAA27230; XP_004467769; QBK47507; KAH0512624; KAH0512624; ELR52172; AEM05834; AEM05851; AIY24744; AIY24804; AIY24755; AIY24754; AIY24757; AIY24813; AIY24821; ADK09717;

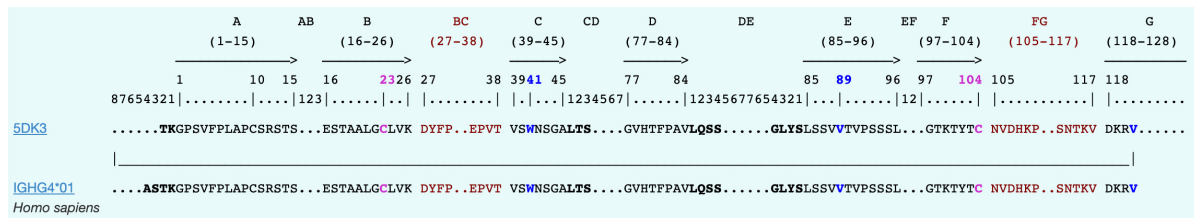
ADK09865; ADK09839; ADK09729; ADK09721; ADK09725; XP_028018162; XP_042090858; AIY24745;
ADK09796; ADK09722; ADK09720; ADK09724; ADK09731; AAA31281; ELW68997; P01845; P01844;
AAK01086; AAM76479; AAO16041; P20767; ADK09758; AIY23702; AET14252; AET14250; AIY24831;
AIY24855; AAO16045; AAO16042; AAO53434; AAO53364; AAO53346; AAO53367; AET14248;
AET14251; ADK09811; ADK09797; ADK09825; ADK09809; AIY24765; AIY24801; AIY24760; AIY24763;
XP_014597487; ADK09714; ADK09768; ADK09763; ADK09854; ADK09833; ADK09726; ADK09826;
ADK09841; ADK09757; AIY24766; AIY24845; AIY24856; ADK09829; AAO53435; ADK09708;
AET14258; ELW68995; AAM76475; AAL37211; AAL37213; AAL37214; ABV02015; ABV02014;
ABV02008; ABV02012; QWC93003; ABV02011; ABV02016; ABV02013; QWC93011; QWC93006;
QWC93001; QWC93009; AAC98629; AAC98624; AAC98625; QWC93020; QWC93005; AAC98628;
AAC98626; AAA49152; AAA49153; AAA86748; AAC59643; AAA86750; AAA50806; AAA86749;
XP_025038876; XP_043385655; XP_043385656; XP_043385733; EMP41349; XP_043353699; EMP40248;
EMP40248; XP_048677958; XP_032620624; XP_032620624; KAG6925585; XP_044842434; XP_032646324;
XP_050774764; XP_023968828; XP_034643422; XP_037771953; XP_048676577; XP_025043132;
XP_024058409; XP_030395824; XP_039355641;

| | C _H 1 domains | | | | | | C _H 3 domains | | | | | | C _L domains | | |
|---------------------------------------|--------------------------|-------------|-----|-------------|-----|-----------|--------------------------|-------------|-----|-------------|-----|-----------|------------------------|-----|--------------------------------------|
| | IgM | IgD/ IgW | IgA | IgG/ IgY | IgE | IgNA R | IgM | IgD/ IgW | IgA | IgG/ IgY | IgE | IgNA R | Igk | Igλ | Total # of sequences per class |
| Mammalia | 79 | 24 | 83 | 164 | 83 | - | 82 | 22 | 69 | 236 | 86 | - | 145 | 220 | 1293 |
| Crocodylia | 4 | 2 | 7 | 9 | - | - | 7 | - | 9 | 11 | - | - | 1 | 4 | 54 |
| Aves | 12 | 2 | 16 | 10 | - | - | 20 | - | 19 | 12 | - | - | 1 | 21 | 113 |
| Testudines | 4 | 10 | - | 8 | - | - | 5 | 6 | - | 9 | - | - | 3 | 23 | 68 |
| Lepidosauria | 5 | 2 | 2 | 5 | - | - | 8 | 2 | - | 5 | - | - | 3 | 11 | 43 |
| Lissamphibia | 5 | 4 | - | 7 | - | - | 8 | 2 | - | 7 | - | - | 4 | 10 | 47 |
| Actinopterygii | 44 | 8 | - | - | - | - | 46 | 9 | - | - | - | - | 59 | 71 | 237 |
| Chondrichthyes | 63 | 55 | - | - | - | 21 | 64 | 20 | - | - | - | 25 | 2 | 7 | 257 |
| Total # of sequences per domain | 738 | | | | | | 789 | | | | | | 585 | | |

Table S1. Number of sequences in the dataset.

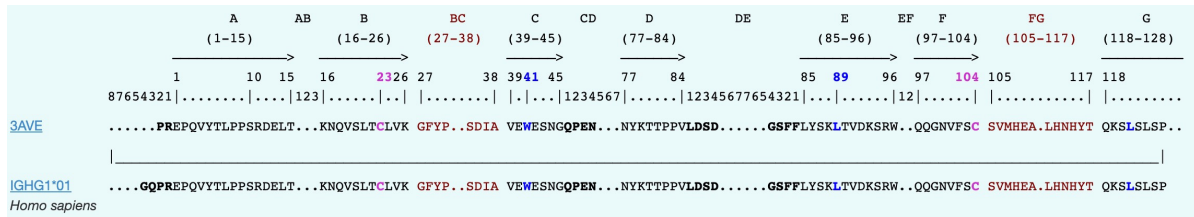
a)

C_H1 domain



b)

C_H3 domain



c)

C_L domain

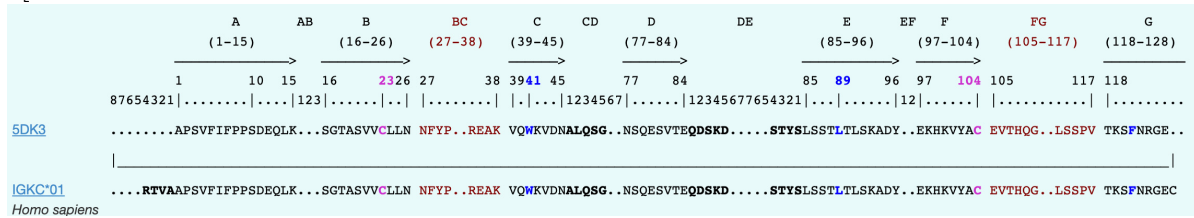


Figure S1. IMGT numeration. a), b), c) C_H1, C_H3 and C_L IMGT alignment, respectively, including one representative structure for each domain. Above the alignment, the IMGT numeration and the corresponding secondary structure annotation. In pink, the residue corresponding to the conserved cysteines and in blue the conserved hydrophobic residues.

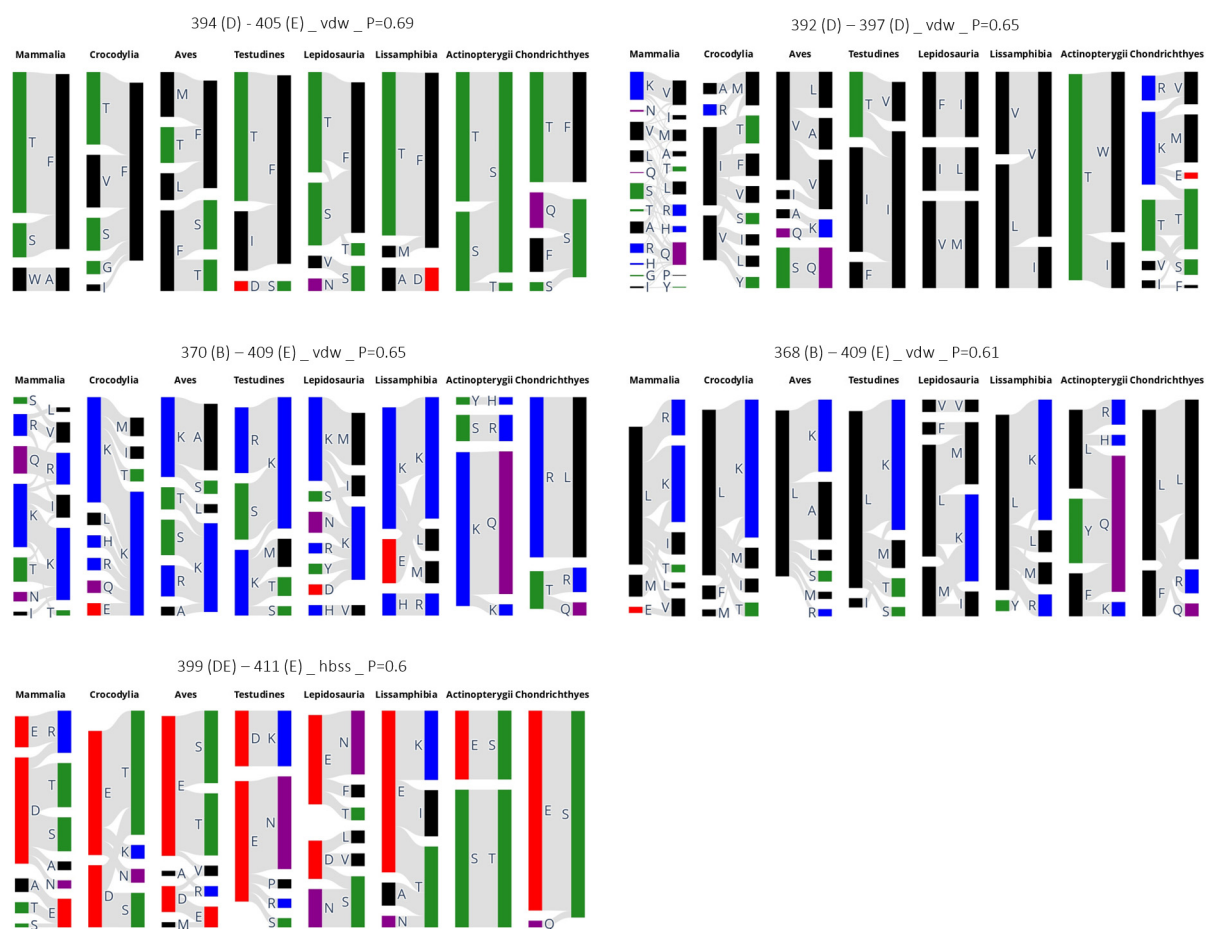
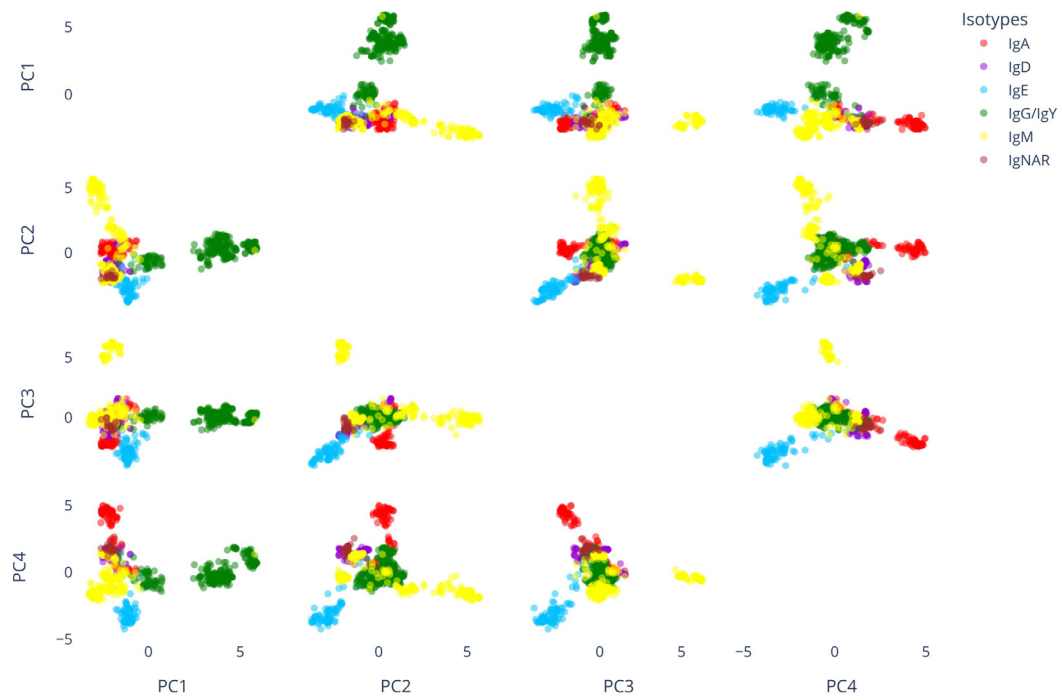


Figure S2. Evolutionary analysis of interdomain contacts. Plots showing the residue pairs present in the two coupled positions. The shown residue pairs are only those that occur in more than 2% of the total number of sequences within each animal class. The colors represent the biochemical property of the residue and are in line with the sequence logos color coding. The title of each plot includes the residue positions, the β -strand/loop where they are in the structure in brackets, the interaction type that the two residues make in the reference structure and the probability obtained from the EVcouplings analysis.

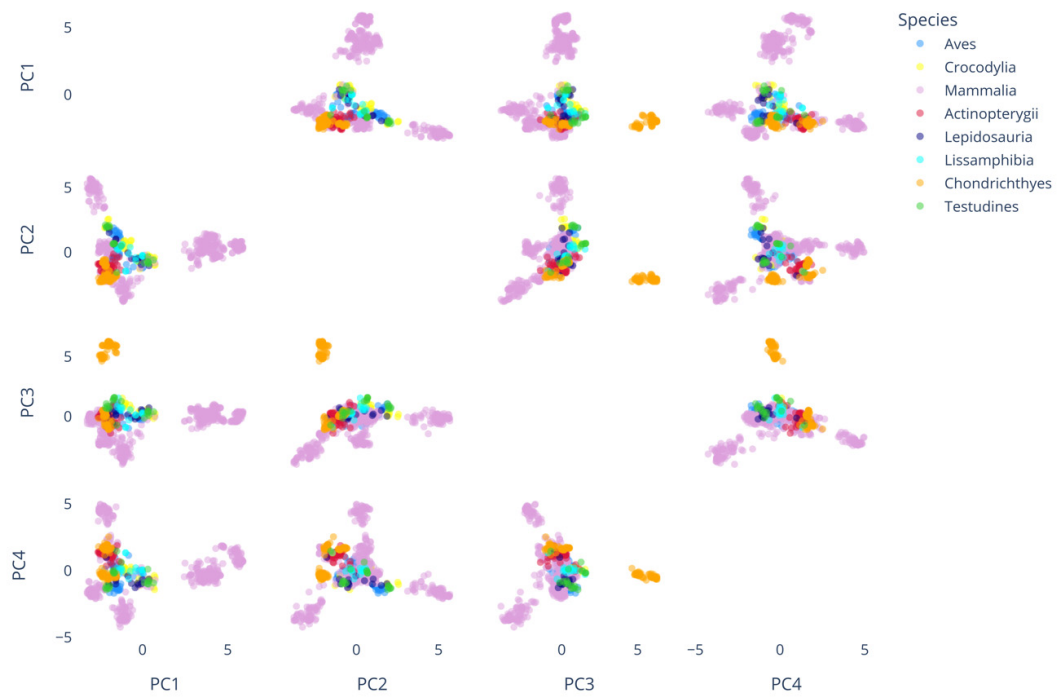
| Residue's pointing direction | Average conservation scores |
|---|--|
| C _H 2 | 0.22 |
| Interdomain | 0.25 |
| Intradomain | 0.31 |
| Solvent | 0.19 |

Table S2. Average conservation score. The conservation scores of the residues pointing in the same direction are averaged and the final value is shown here.

a) C_H3 domains



b) C_H3 domains



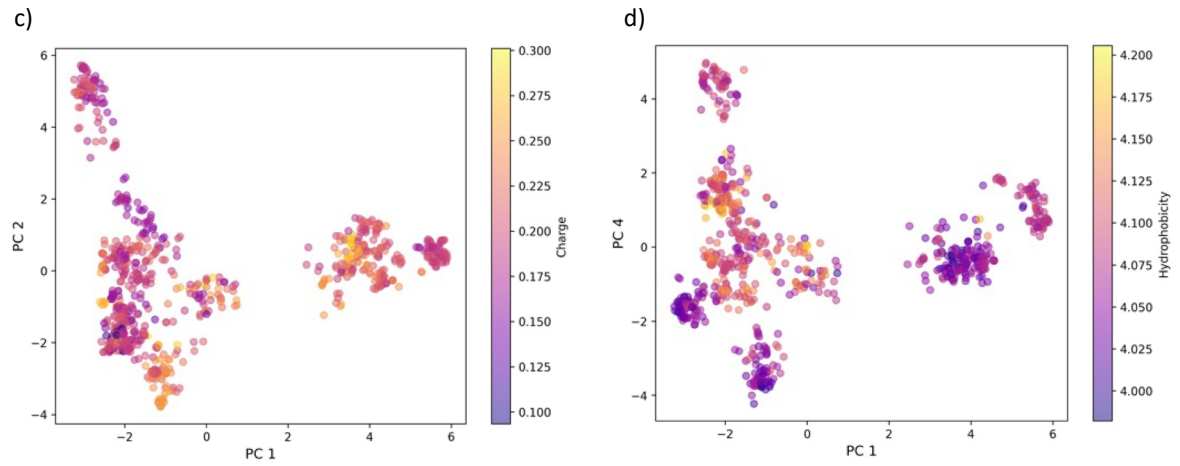


Figure S4. PCA analysis of the CH3 domains sequences. **a)** The PCA separation of the Ig isotype in the first four PCs space is shown. **b)** The same PCA space as in Figure S4a is colored according to the animal class that the sequence belongs to. **c)** Projection of the normalized charges in the PC1-PC2 plot. **d)** Projection of the normalized hydrophobicity value in the PC1-PC4 plot.

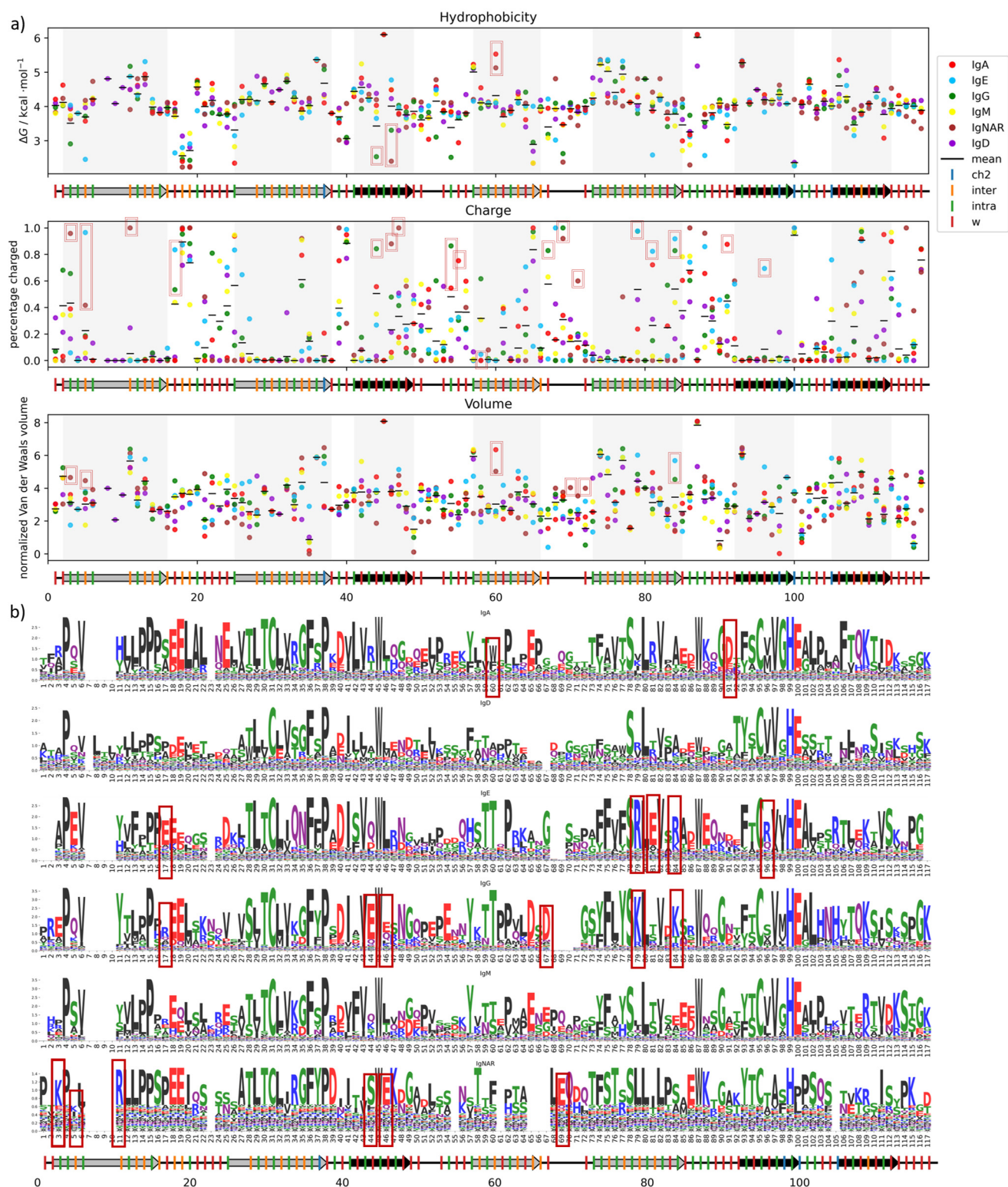
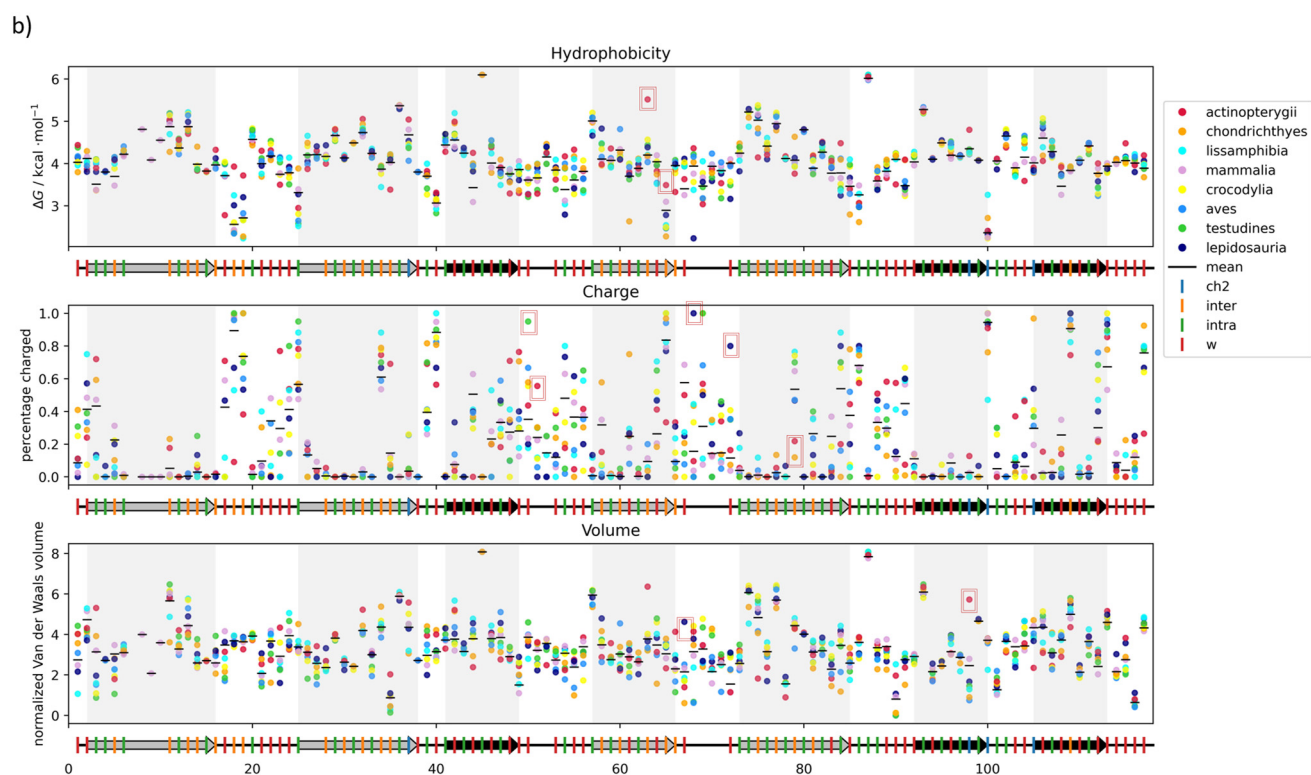
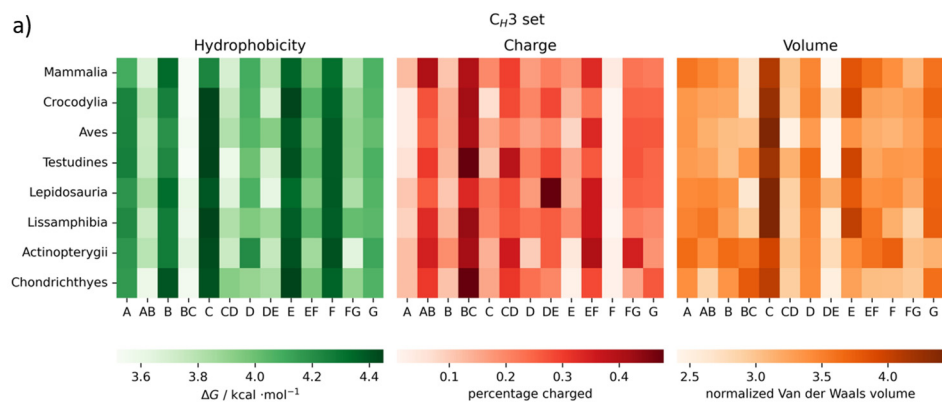


Figure S5. Biophysical properties of Ch3 domains in different isotypes. **a)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each sequence position for each isotype. Below each subplot, a representation of the secondary structure of an exemplary Ch3 domain: the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain and blue, towards the Ch2; a

missing tick means that the reference structure presents a gap in that position. In red squares the points that differ the most. **b)** Sequence logos of each isotype. The secondary structure is shown below. In red squares, the residues that differ the most.



c)

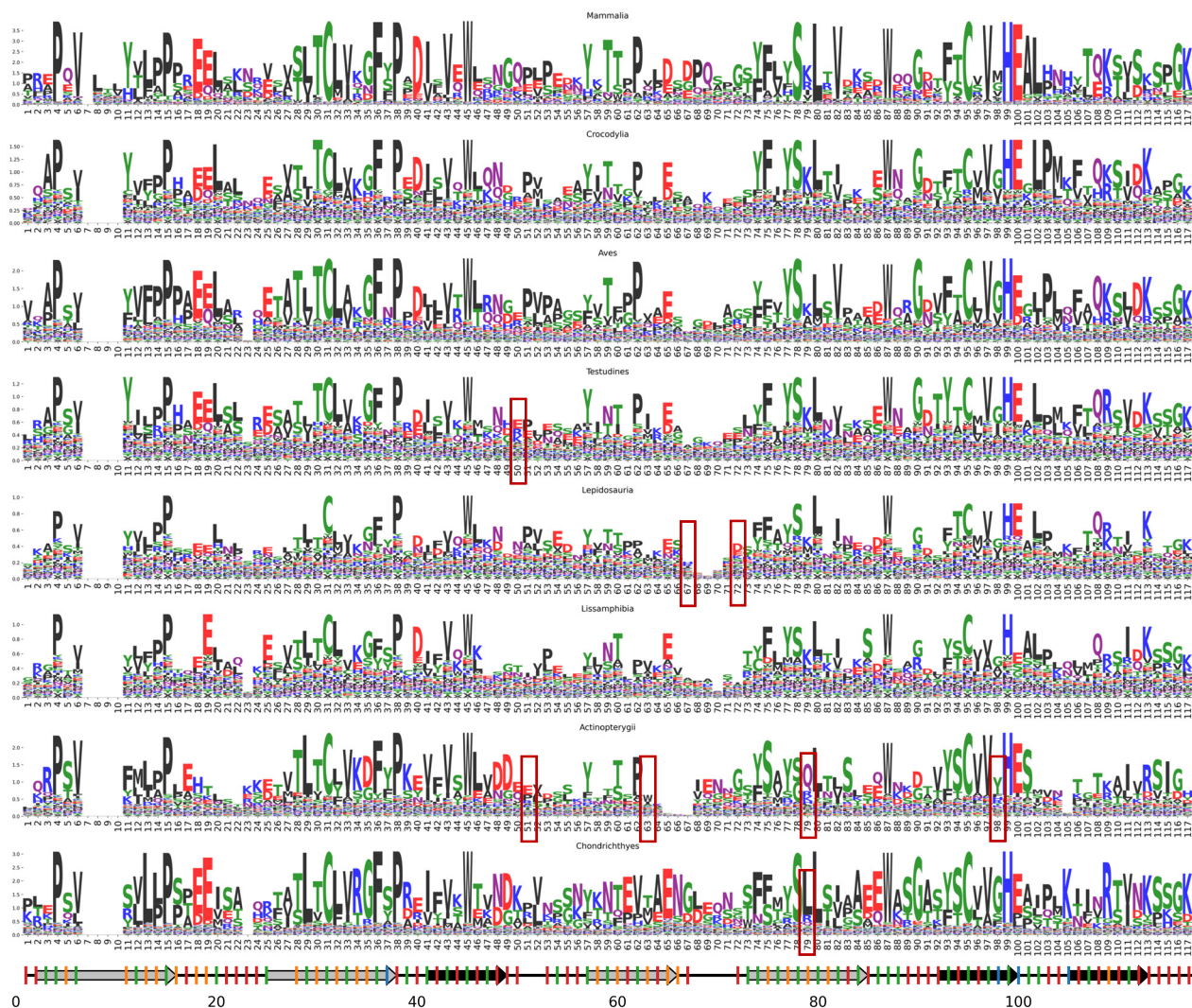
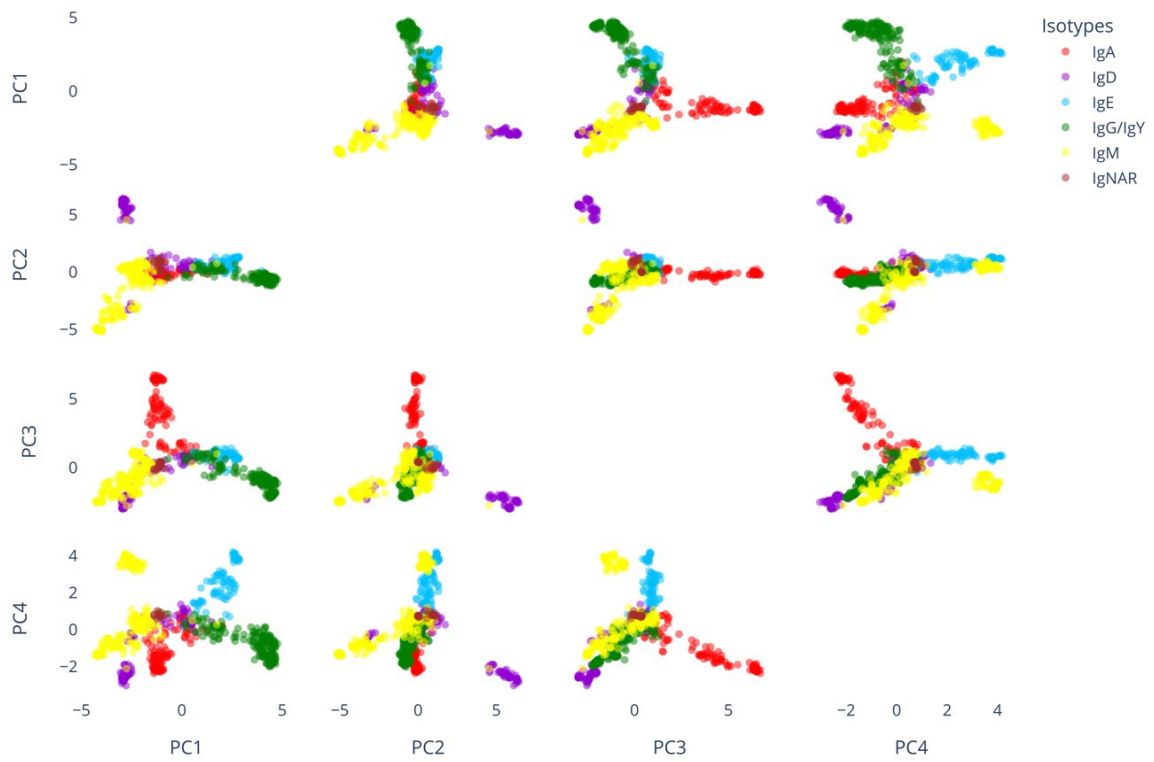


Figure S6. Biophysical properties of CH3 domains in different animal classes. **a)** Heatmap showing the occurrence of the biophysical property (hydrophobicity, charge and volume) in each secondary structure element for each animal class. **b)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each sequence position for each animal class. Below each subplot, a representation of the secondary structure of an exemplary CH3 domain: the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain and blue, towards the CH2; a missing tick means that the reference structure presents a gap in that position. In red squares the points that differ the most. **c)** Sequence logos of each animal class. The secondary structure is shown below. In red squares, the residues that differ the most.

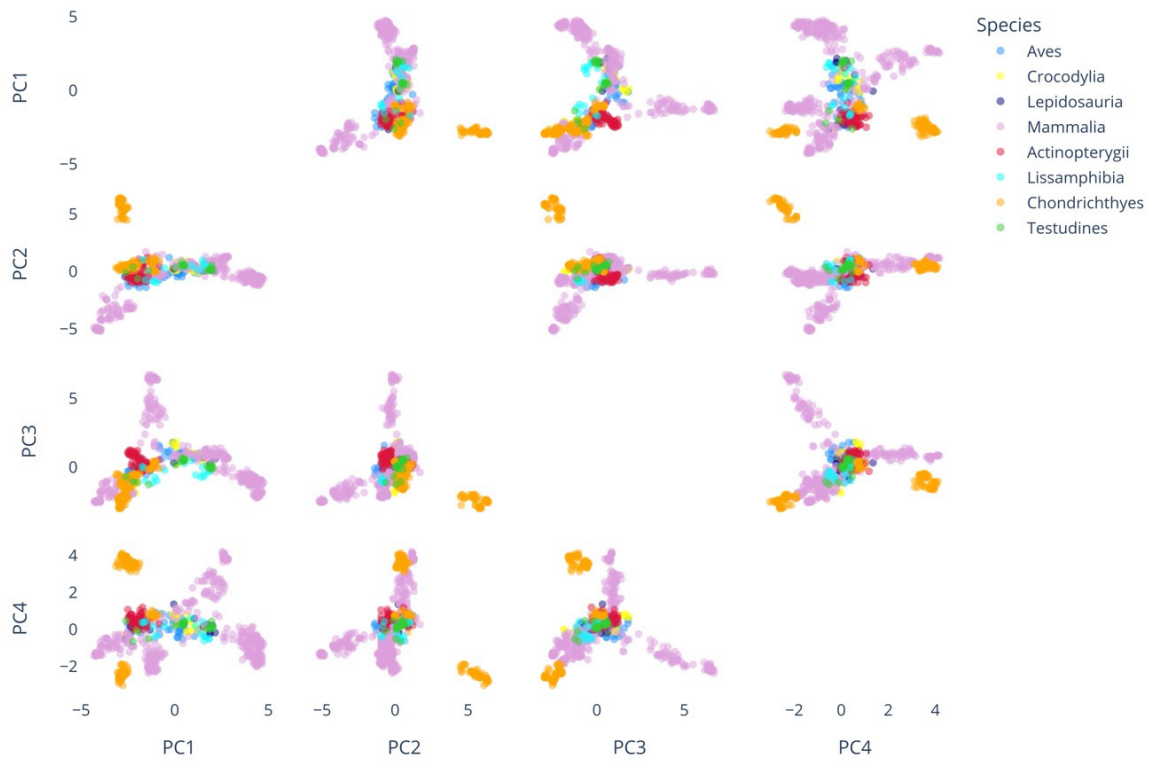
a)

C_H1 domains



b)

C_H1 domains



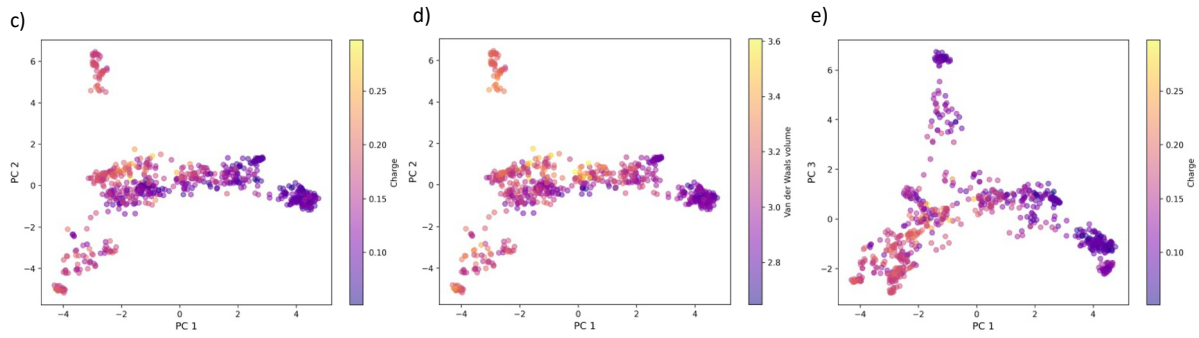


Figure S7. PCA analysis of the C_H1 domains sequences. **a)** The PCA separation of the Ig isotype in the first four PCs space is shown. **b)** The same PCA space as in Figure S7a is shown, colored according to the animal class that the sequence belongs to. **c)** Projection of the normalized charges in the PC1-PC2 plot. **d)** Projection of the normalized van der Waals volume values in the PC1-PC2 plot. **e)** Projection of the normalized charges in the PC1-PC3 plot.

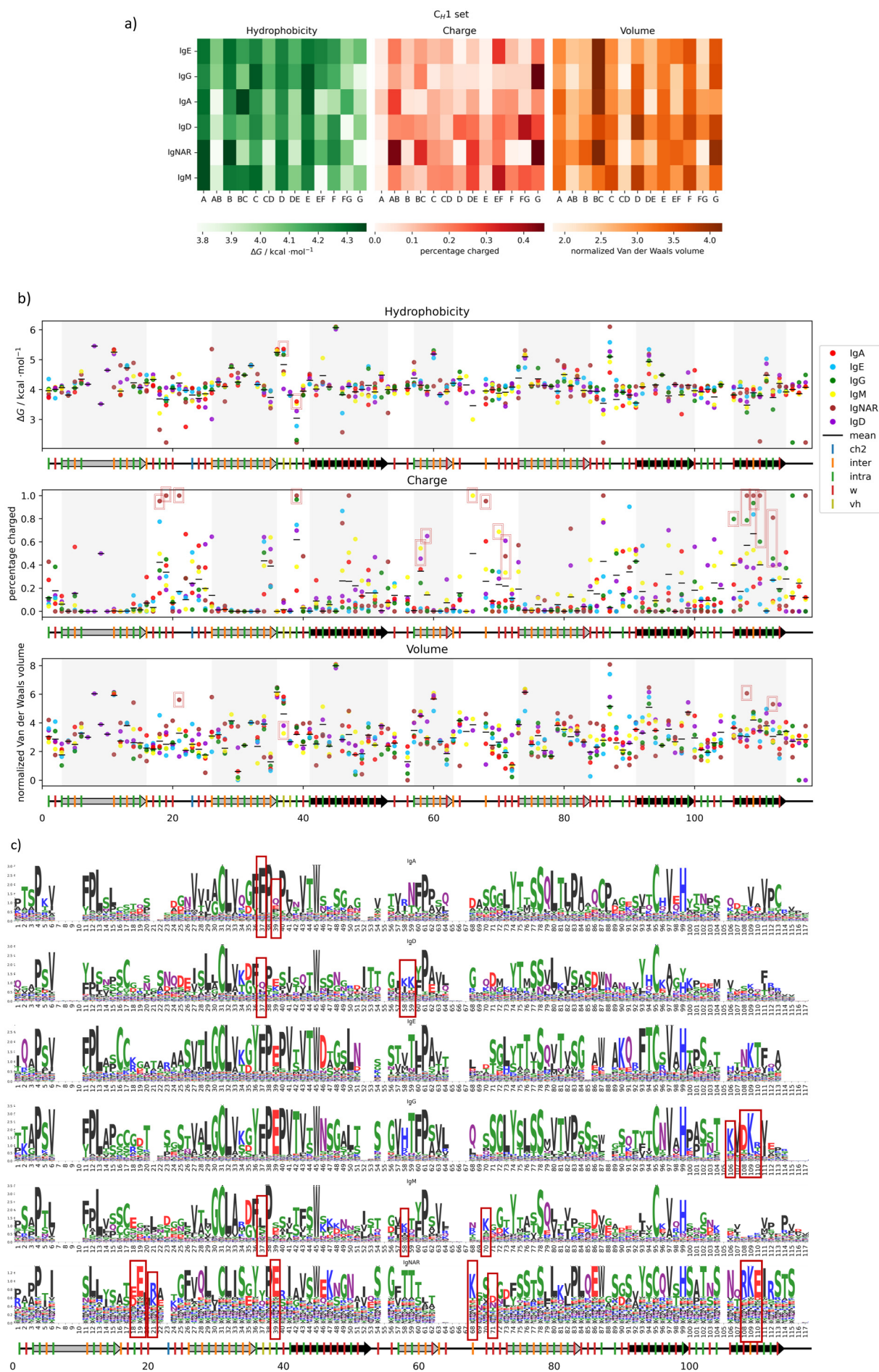


Figure S8. Biophysical properties of C_H1 domains in different isotypes. **a)** Heatmap showing the occurrence of the biophysical property (hydrophobicity, charge and volume) in each secondary structure element for each Ig isotype. **b)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each sequence position for each Ig isotype. Below each subplot, a representation of the secondary structure of an exemplary C_H1 domain: the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain, blue, towards the C_H2, and yellow towards the variable domain; a missing tick means that the reference structure presents a gap in that position. In red squares the points that differ the most. **c)** Sequence logos of each Ig isotype. The secondary structure is shown below. In red squares, the residues that differ the most.

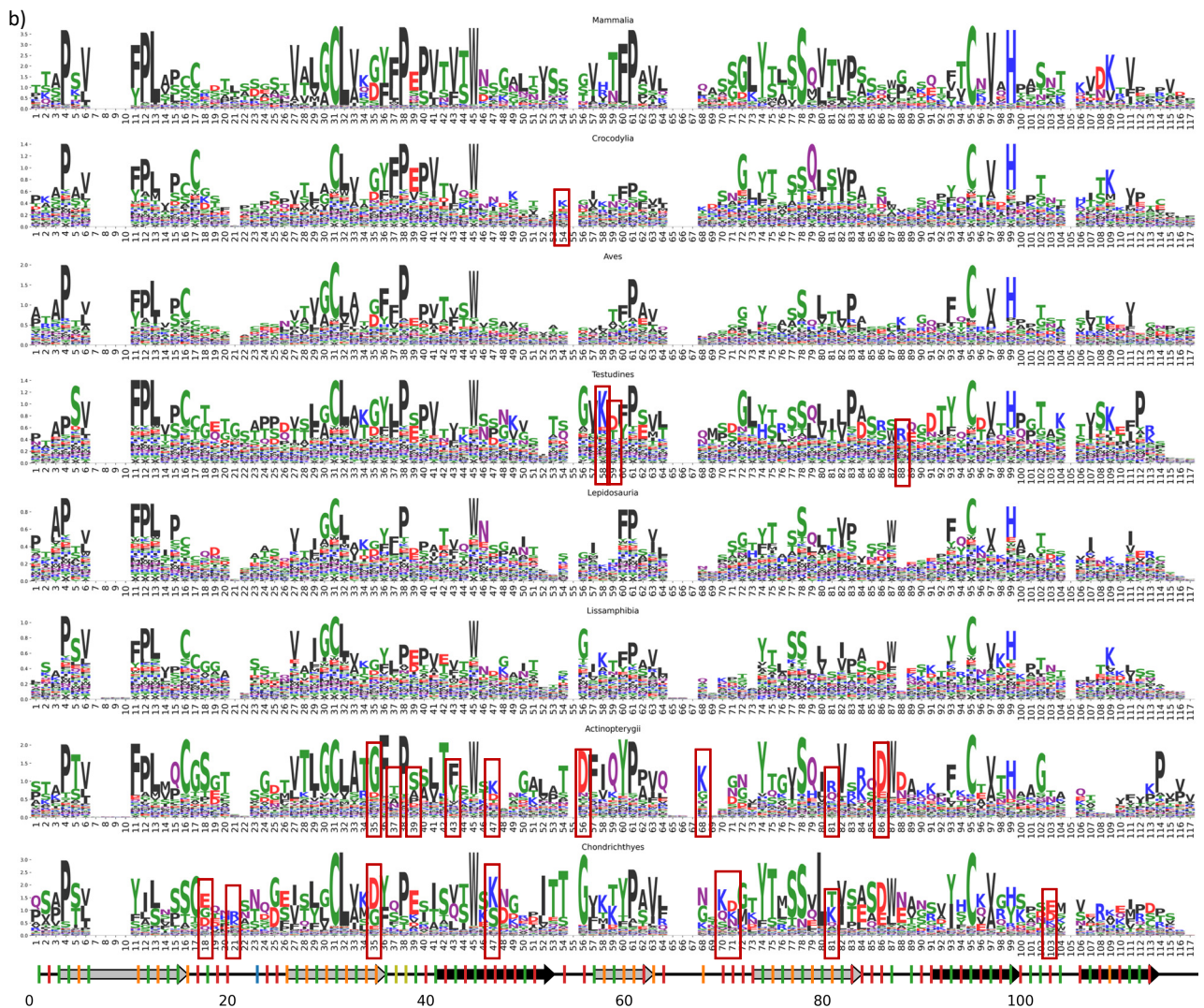
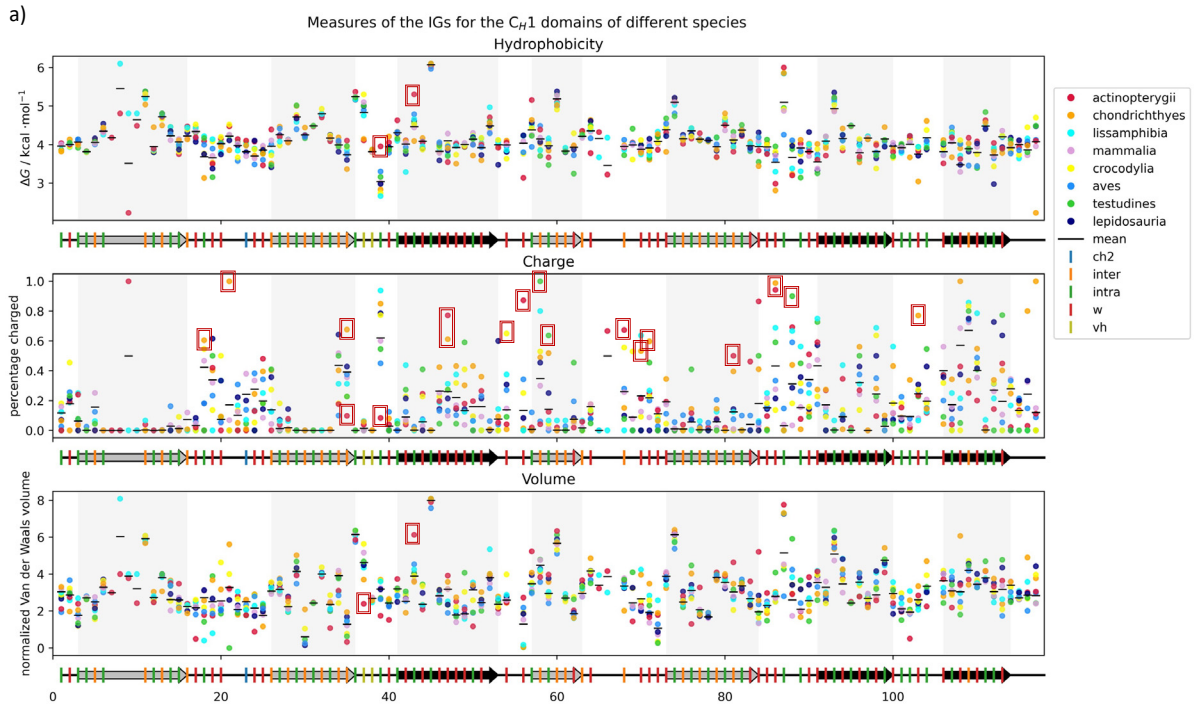


Figure S9. Biophysical properties of C_H1 domains in different animal classes. **a)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each sequence position for each animal class. Below each subplot, a representation of the secondary structure of an exemplary C_H1 domain: the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain, blue, towards the C_H2, and yellow towards the variable domain; a missing tick means that the reference structure presents a gap in that position. In red squares the properties that differ the most. **b)** Sequence logos of C_H1 domain in each animal class. The secondary structure is shown below. In red squares, the residues that differ the most.

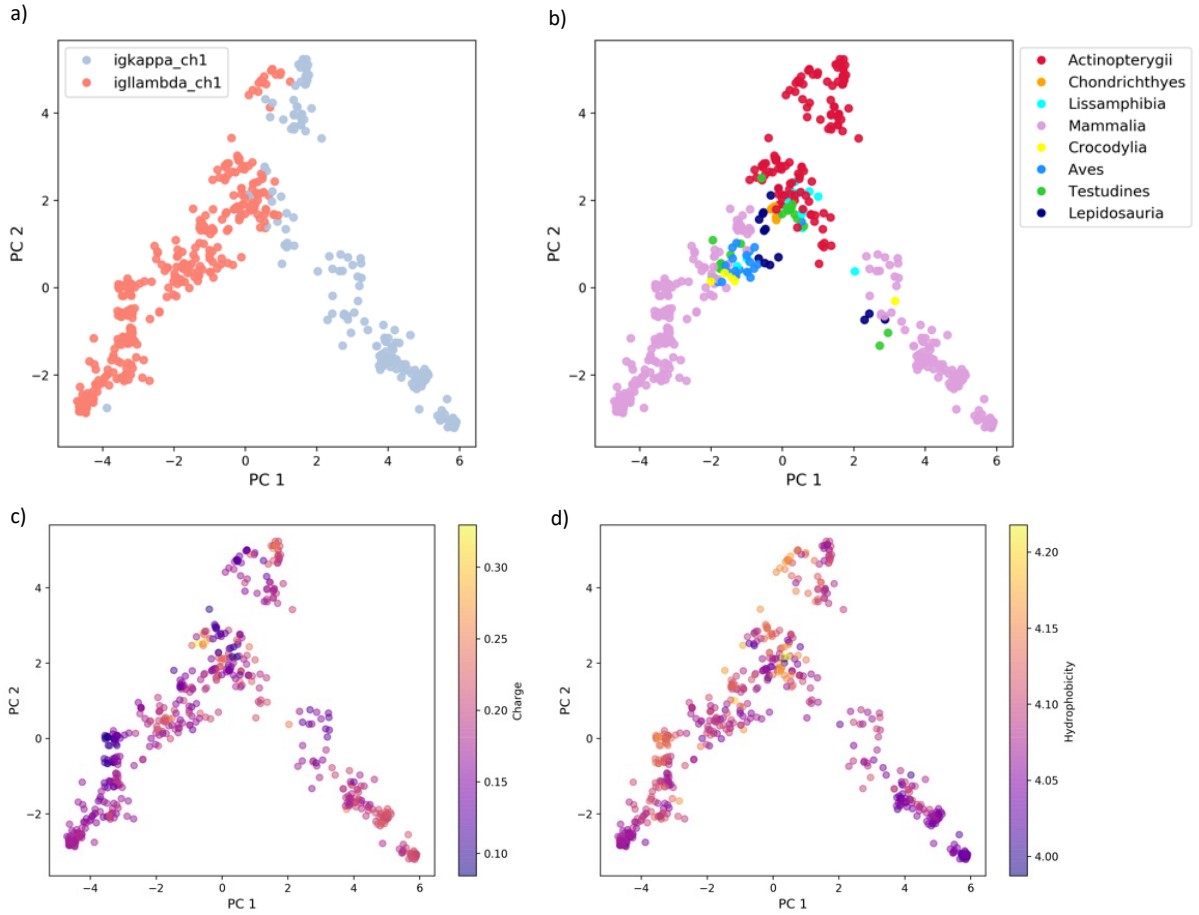


Figure S10. PCA analysis of the C_L domains sequences. **a)** The PCA separation of the Ig light chain isotypes. **b)** The same PCA space as in Figure S10a is shown, colored according to the animal class that the sequence belongs to. **c)** Projection of the normalized charges in the PC1-PC2 plot. **d)** Projection of the normalized hydrophobicity values in the PC1-PC2 plot.

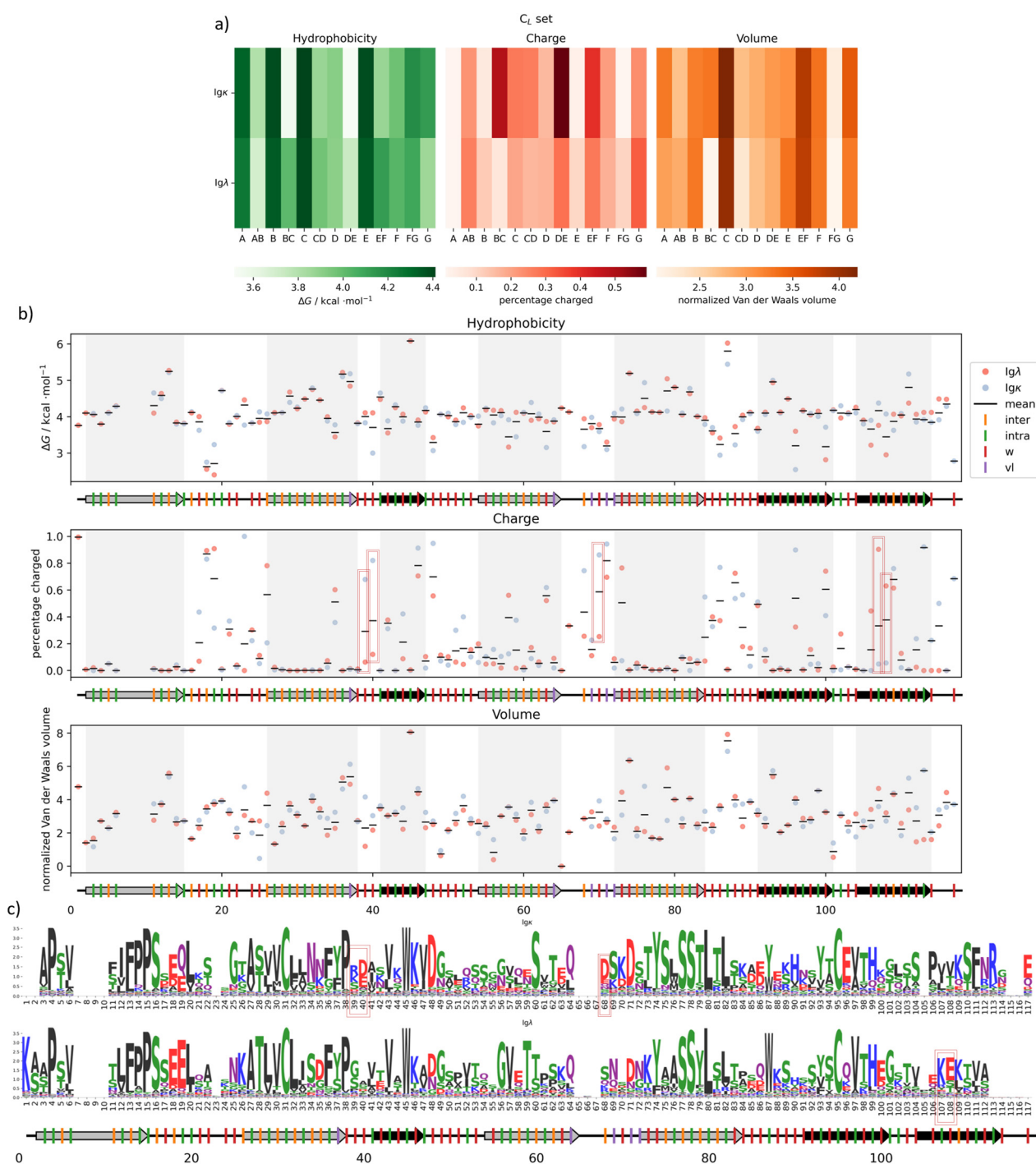
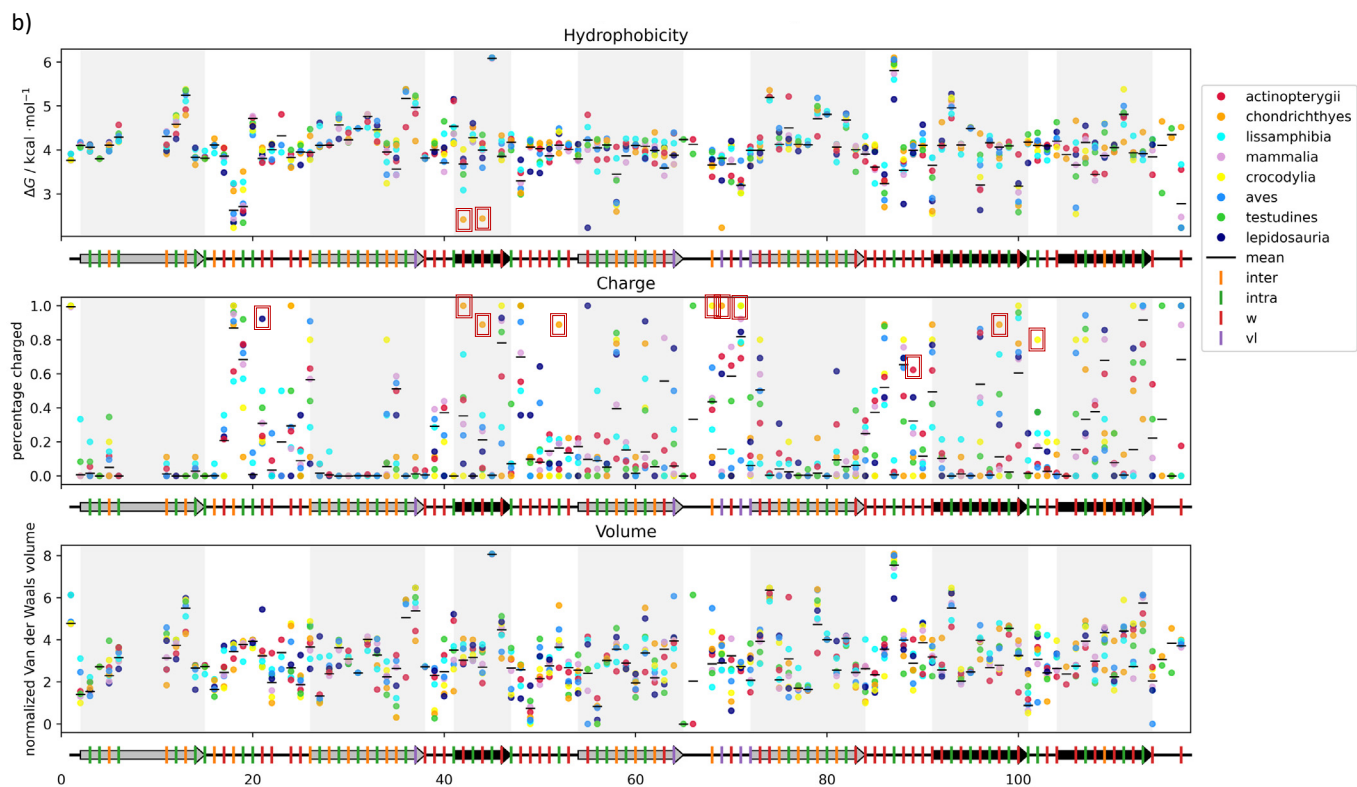
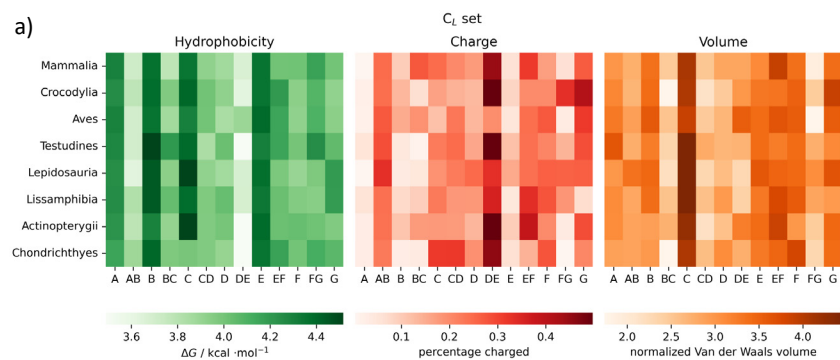


Figure S11. Biophysical properties of C_L domains in different isotypes. **a)** Heatmap showing the occurrence of the biophysical property (hydrophobicity, charge and volume) in each secondary structure element for each Ig light chain isotype. **b)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each sequence position for each Ig light chain isotype. Below each subplot, a representation of the secondary structure of an exemplary C_L domain (PDB: 5DK3): the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain, and purple towards the variable domain; a missing tick means that the reference structure presents a gap in that position. In red squares the point that differ the most. **c)** Sequence logos of each Ig light chain isotype. The secondary structure is shown below. In red squares, the residues that differ the most.



c)

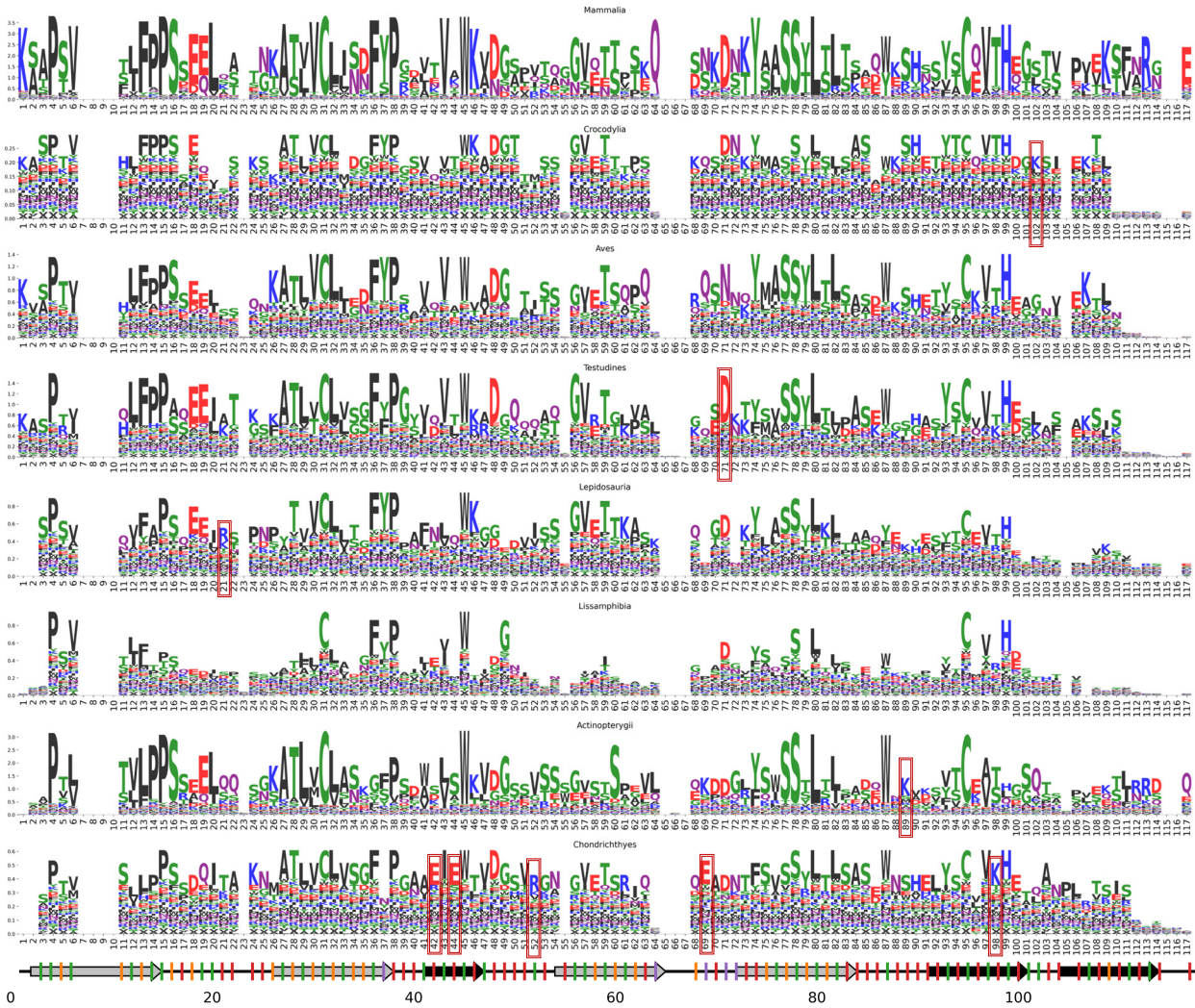


Figure S12. Biophysical properties of CL domains in different animal classes. **a)** Heatmap showing the occurrence of the biophysical property (hydrophobicity, charge and volume) in each secondary structure element for each animal class. **b)** Scatter plot showing the average value of hydrophobicity, charges and van der Waals volume, in each CL domain sequence position for each animal class. Below each subplot, a representation of the secondary structure of an exemplary CL domain: the light grey arrows represent the strands that point towards the facing domain, instead the black ones are the strands that point towards the solvent; the lines are the loops. The ticks on the secondary structure show where the residue points: if red, it points towards the solvent, green, in-between the β -sheets, orange, in the interface with the facing domain, and purple towards the variable domain; a missing tick means that the reference structure presents a gap in that position. In red squares the points that differ the most. **c)** Sequence logos of CL domain alignments for each animal class. The secondary structure is shown below. In red squares, the residues that differ the most.